CLINICAL AND ELECTROPHYSIOLOGICAL PROFILE OF VESTIBULAR FUNCTION IN PARKINSON DISEASE

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CERTIFICATE

This is to certify that the dissertation entitled "**CLINICAL AND ELECTROPHYSIOLOGICAL PROFILE OF VESTIBULAR FUNCTION IN PARKINSON DISEASE"** is a bonafide record of work done by **Dr.RAVICHANDRAN.R** in the Institute of Neurology, Rajiv Gandhi Government General Hospital & **MADRAS MEDICAL COLLEGE, CHENNAI** in partial fulfillment of the Tamilnadu Dr.MGR Medical University rules and regulations for the award of **D.M. (NEUROLOGY)** degree under my direct guidance and supervision during the academic year **2011-2014**.

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DECLARATION

I solemnly declare that this dissertation titled **"CLINICAL AND ELECTROPHYSIOLOGICAL PROFILE OF VESTIBULAR FUNCTION IN PARKINSON DISEASE"** is done by me in the Institute of Neurology, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai under the guidance and supervision of **Prof. Dr. R.LAKSHMI NARASIMHAN, MD., DipNB., D.M., DipNB.,** Professor of Neurology, Institute of Neurology, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai. This dissertation is submitted to the Tamil Nadu Dr.MGR Medical University, Chennai in partial fulfillment of the university requirements for the award of the degree of D.M. Neurology.

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CONTENTS

ABSTRACT

Postural instability, dysequilibrium, freezing of gait and the consequential falls are among the most disabling manifestations of Parkinson's disease. Postural instability in PD results from abnormalities in sensorimotor integration. The role of vestibular otolith function in dysequilibrium in PD is still not clear. We assessed the clinical profile and vestibular evoked myogenic potential (VEMP) in patients with Parkinson disease. We have found that bilaterally absent VEMPs are a pointer to the otolithic vestibular dysfunction in patients with Parkinson's disease. Peak latencies of the p13 and n23 are not prolonged in patients with Parkinson's disease and VEMPs in patients with Parkinson's disease seem to follow an "all or none" response either with a present or absent response. Cervical VEMPs in patients with Parkinson's disease correlate significantly with falls and postural instability. Cervical VEMPs may serve as a predictor or marker of falls and postural instability in patients with Parkinson's disease.

INTRODUCTION

Postural instability, dysequilibrium, freezing of gait and the consequential falls are among the most disabling manifestations of Parkinson's disease. About 38 to 87% of patients with parkinsonian experience fall. Recurrent falls also occur at a rate of about 50% in 1year.[1] After the first fall the survival in PD drops to that of atypical parkinsonian syndromes.[2]

Postural stability depends of proper central integration of vestibular, proprioceptive and visual signals and institution of appropriate anticipatory and adaptive postural responses during perturbations in balance.

Postural instability in PD results from abnormalities in sensorimotor integration. The role of vestibular otolith function in dysequilibrium in PD is still not clear. The function of saccular part of otolith can be assessed by cervical vestibular evoked myogenic potentials (VEMP)

We have proposed to study the role of dysfunction of saccular connections in PD.

AIMS AND OBJECTIVES

The aim of this study is,

- To assess the clinical profile and vestibular evoked myogenic potential (VEMP) in patients with Parkinson disease.
- To compare vestibular evoked myogenic potential (VEMP) in patients with Parkinson disease and healthy controls.
- To study the abnormalities in vestibular evoked myogenic potential (VEMP) in patients with Parkinson disease.
- To study the correlation between postural instability and vestibular evoked myogenic potential (VEMP) in patients with Parkinson disease.

REVIEW OF LITERATURE

PARKINSONISM

Parkinsonism is a syndrome which manifests as a mixture of the six cardinal features namely, rest tremor, rigidity, bradykinesia, loss of postural reflexes, flexed posture, and freezing. Parkinsonism is defined clinically as definite, probable, and possible by a combination of these signs (Table-1).

Table - 1 : Diagnostic criteria for Parkinsonism	
1. Tremor-at-rest 2. Bradykinesia 3. Rigidity 4. Loss of postural reflexes 5. Flexed posture 6. Freezing (motor blocks)	
Definite	At least two of these features must be present, one of them being 1 or 2
Probable	Feature 1 or 2 alone is present
Possible	At least two of features 3 to 6 must be present

The most common cause of Parkinsonism is the idiopathic Parkinson disease (PD).

This unique clinical entity was first recognized by James Parkinson in 1817.

Diseases that cause Parkinsonism other than Parkinson's disease are classified as

- Secondary
- Parkinsonism-plus syndromes
- Heredodegenerative disorders

Box-1 : Features suggesting a diagnosis other than Parkinson's disease
Symmetrical signs
Falls within the first year
Early or prominent dementia
Early gait disorder
Early autonomic failure
Sleep apnea
Inspiratory stridor
Apraxia
Alien limb
Cortical sensory loss
Wheelchair dependence within 5 years

Certain clinical features serve as a "red flag" pointing to a diagnosis other than PD (Box-1).

PARKINSON'S DISEASE

Parkinson's disease is the second commonest neurodegenerative disease after Alzheimer's disease. An estimated 5 million persons in the world are affected by this disorder. The mean age of onset of Parkinson's disease is about 60 years. However, the disease can be seen in persons in their third decade and even

younger. The incidence of Parkinson's disease increases with age. The prevalence of Parkinson's disease will dramatically increase in future based on the data from projected population demographics.

Clinical manifestations of Parkinson's disease include rest tremor, bradykinesia, rigidity, and gait impairment. These features are known as the "cardinal features" of Parkinson's disease. Freezing of gait, postural instability, autonomic disturbances, sensory alterations, speech difficulty, mood disorders, sleep dysfunction, cognitive impairment, and dementia are other common presentations of the disease. (Table-2)

Table - 2 : Clinical Features of Parkinson's Disease		
Motor features		**Non - motor features**
Cardinal features	**Other features**	
Rest tremor	Masked facies (hypomimia)	Anosmia
Bradykinesia	Reduced eye blink	Cognitive impairment
Rigidity	Soft voice (hypophonia)	Mood disorders
Gait disturbance/	Dysphagia	Sleep disturbances
Postural instability	Micrographia	Sensory disturbances
	Freezing of gait	Autonomic disturbances
		Gastrointestinal disturbances

The pathological features of Parkinson's disease include degeneration of dopaminergic neurons in the substantia nigra pars compacta , reduced striatal dopamine with intra cytoplasmic proteinaceous inclusions known as Lewy bodies. While the dopamine system is predominantly involved neuronal degeneration with inclusion bodies is also seen in the cholinergic neurons of the nucleus basalis of Meynert, nor-adrenergic neurons of the locus coeruleus, serotoninergic neurons in the raphe nuclei of the brainstem, and neurons of the olfactory

system, cerebral hemispheres, spinal cord, and peripheral autonomic nervous system.

Pathology in Parkinson's disease begins in the olfactory system, peripheral autonomic nervous system, and dorsal motor nucleus of the vagus nerve in the lower brainstem. It then spreads sequentially to involve upper brainstem and cerebral hemispheres. The dopaminergic neurons are usually affected in mid stage of the disease. The symptoms reflecting the involvement of non dopaminergic degeneration such as anosmia, constipation, cardiac denervation, and rapid eye movement behaviour sleep disorder appears before the onset of motor features of the disease.

Parkinson's disease is heterogeneous with regards to the clinical symptomatology, natural progression, and the complications of the disease. The following clinical subtypes of PD are recognised now.[3]

(1) Young age at onset and slow disease progression

(2) Old age at onset and rapid disease progression

(3) Tremor dominant

(4) Postural instability and gait difficulty (PIGD)

Patients predominantly manifesting with axial symptoms, such as dysarthria, dysphagia, freezing of gait, and loss of equilibrium, significantly disabled by their disease compared to those with predominant limb manifestations. These patients in whom axial symptoms predominate often have poor prognosis.[4]

Diagnosis of Parkinson's disease

Several criteria have been developed for the diagnosis of Parkinson's disease. Of these the UK Parkinson's Disease Society Brain Bank criteria is often used in various clinical-pathologic studies(Table-3).[5]

Table - 3 : UK Parkinson's Disease Society Brain Bank's clinical criteria for the diagnosis of probable Parkinson disease	
Step 1	1. Bradykinesia 2. At least one of the following criteria: A. Rigidity B. 4–6 Hz rest tremor C. Postural instability not caused by primary visual, vestibular, cerebellar, or proprioceptive dysfunction
Step 2	Exclude other causes of parkinsonism
Step 3	At least three of the following supportive (prospective) criteria: 1. Unilateral onset 2. Rest tremor present 3. Progressive disorder 4. Persistent asymmetry affecting side of onset most 5. Excellent response (70–100%) to levodopa 6. Severe levodopa-induced chorea (dyskinesia) 7. Levodopa response for 5 years or more 8. Clinical course of 10 years or more

Symptoms such as rest tremor, walking difficulty, walking slowly, and difficulty rising from chair are highly specific (93.8–95.9%), but lack sensitivity (35.9-49.1%). Whereas the other parkinsonian manifestations like olfactory dysfunction and micrographia are more sensitive but less specific.[6]

Rating and staging of PD

Several clinical rating scales exist for quantitative analysis of the severity of various parkinsonian symptoms and signs.[7–9]

Unified Parkinson's disease Rating Scale (UPDRS)

Hoehn–Yahr Staging Scale (Table- 4)

Schwab–England Scale of activities of daily living

Short Parkinson's Evaluation Scale (SPES)

Scale for Outcomes in Parkinson's disease (SCOPA)

Although the UPDRS and Hoehn and Yahr staging have some limitations this is the most frequently used instrument in clinical and research trials.

Table - 4 : Hoehn and Yahr Stage - Modified scale	
Stage	**Disease State**
0	No signs of disease
1.0	Unilateral disease
1.5	Unilateral plus axial involvement
2.0	Bilateral disease without impairment of balance
2.5	Mild bilateral disease with recovery on pull test
3.0	Mild to moderate bilateral disease, some postural instability, physically independent
4.0	Severe disability, still able to walk or stand unassisted
5.0	Wheelchair bound or bedridden unless aided

Postural instability and falls in PD

Postural instability, dysequilibrium, freezing of gait and the consequential falls are among the most disabling manifestations of Parkinson's disease.

About 38 to 87% of patients with parkinsonian experience fall. Recurrent falls also occur at a rate of about 50% in 1year.[1] After the first fall the survival in PD drops

to that of atypical parkinsonian syndromes.[2] The predictive factors of falls are as follows

- Previous fall
- Fear of falling
- Disease duration and severity
- Abnormal axial posture and tone
- Cognitive impairment
- Decrease in arm swing (unilateral or bilateral)
- Presence of dyskinesia
- Anti parkinsonian treatment.[10]

Situations that precipitate a fall include posture changes (during a half-turn), or performing double task demand activities.[11] Vestibular and proprioceptive deficits are also reported in PD, which could lead to dysequilibrium .[12]

Although postural instability in PD is evaluated with the pull-retropulsion test, variability exists in the execution of the test and its reproducibility is low. Therefore, this is not a sensitive test to detect early fallers.[12] Clinical testing for postural instability does not reliably predict the risk of falls.[1] Some non-specific

scales that have been used to evaluate the balance and risk of falls in PD patients include

- Tinetti score
- Berg Balance Scale
- Timed Up and Go test
- Functional Gait Assessment
- Balance Evaluation System Test
- Rapid Assessment of Postural Instability in PD

These tests showed good sensitivity in detecting fallers among PD patients.[10,13]

POSTURAL CONTROL

An erect standing posture can be affected by perturbations to the vestibular, visual, and proprioceptive sensory systems. Postural control is achieved by an effective integration of sensory information about the body and limb position and the visuospatial environment.[14] Central nervous system is presumed uses a ‘‘sensory reweighting’’ strategy during integration of sensory inputs thereby compensating for loss or inaccurate input from one or more sensory modality. [15]

Role of basal ganglia in postural control

Basal ganglion plays a complex role in the control of posture and locomotion. It is been shown to be involved in multiple aspects of postural control including

- Sensory channel integration
- Selection of automatic postural reactions
- Flexibility and adaptability in motor control
- Regulation of muscle tone
- Modulating the impact of cognitive factors on gait and balance.[16]

Pathophysiology of postural instability in Parkinson's disease

Standing balance

During unperturbed standing spatial, frequency, and velocity characteristics of body sway is abnormal in PD**.** In the event of external motor or sensory perturbations during standing, there is impairment in the generation of normal postural reactions in patients with PD.

Central postural set, which refers to the ability of the nervous system to modulate the adaptive or anticipatory postural adjustments are found to be impaired in PD.[17]

Dopaminergic therapies do not have any significant impact on these adaptive postural reactions.

Gait

The inherent ability to regulate gait as reflected by gait variability is often abnormal in PD. Other gait abnormalities reported in patients with PD are

- Reduced walking speed and short steps
- Stooped posture due to hypertonia
- gait shuffling with reduced ground clearance and festination
- Reduced joint angular excursions
- Increased gait variability
- Gait facilitation by simple sensory cueing
- Gait initiation:
    - reduced propulsion forces

- reduced lateral body displacement

- Turning:
  - longer times to turn off postural muscles
  - increased number of steps required to turn[18]

Vestibular dysfunction in Parkinson's disease

The contribution of vestibular dysfunction to instability in patients with PD remains uncertain. Studies analyzing the different parts of the vestibular system for their role in postural instability in PD have come with mixed results.

Tests that specifically assess the lateral semicircular canals and their connections (rotational chair test and caloric test) were shown to be abnormal in PD. However further studies have demonstrated that this finding is inconsistent.[19–21]

Studies testing the tilting table to examine the postural reflexes (an otolith reaction) showed abnormalities during the tonic phase. However, it remains to be proven that tilting table response specifically assesses the otolith function.[22]

Galvanic stimulation of the vestibular nerve (activates utricular part of vestibulospinal reflex) did not show any differences in postural sway between patients with PD and the controls.[23]

Vestibular myogenic potentials (VEMP) evoked by auditory clicks is a recently added tool in the assessment of otolith function.[24–28]

VESTIBULAR EVOKED MYOGENIC POTENTIAL (VEMP*)*

Vestibular-evoked myogenic potential (VEMP) is a relatively new technique in the evaluation of vestibular function. "VEMP is a short latency myogenic response evoked by brief pulses of air conducted sound, bone-conducted vibration or electrical stimulation and recorded using surface electrodes placed over the muscles".[29]

History of VEMP

Inner ear is composed of two divisions, one function as an organ of balance (three semicircular canals, saccule and the utricle) and the other serves the auditory function (cochlea). From the point of evolution saccule of the inner ear is the earliest to develop among the other structures in the membranous labyrinth of the inner ear.[30] In primitive species like fish, saccule acts as an acoustic organ in the absence of cochlea. Moreover, there is evidence that human saccule has some preserved ancestral acoustic sensitivity. Since the sound levels required for eliciting VEMP is high it may be difficult to conclude whether the response is due

to vestigial acoustic function of the saccule or a mechanically induced vestibular response transmitted through endolymph compression in response to the sound stimuli.[31]

Short latency responses using auditory clicks were recorded at inion by Yoshie and Okudaira in 1969 and these responses were initially presumed to be of cortical origin.[32] Bickford et al demonstrated that these "inion response" were in fact myogenic (indicating that the origin of the response is from averaged electrical activity of muscle recorded by EMG) and the amplitude of the response was related to muscle tension and abolished by curarisation.[33] The inion response was distinct from the cochlea mediated ‘‘vertex response” to sound. These sound induced myogenic responses have been elicited in deaf ear with intact vestibular function confirming its vestibular origin. Dissociation from the caloric response (mediated by semi circular canal), effects of the ‘‘tack” operation (a procedure that damages the saccule) and the evidence of tuning to 250 Hz, suggests that the saccule is the end organs for these myogenic response.[29]

In 1994, Colebatch et al revised the previous recording procedures by using surface electrodes on the sternocleidomastoid (SCM) instead of recording from the inion. These responses were initially called “click-evoked vestibulo-collic

responses".[34] At present "vestibular evoked myogenic potentials" is the preferred terminology as the stimulus is similar to conventional (neural) evoked potentials and the response is myogenic.[29,31] Other evoked myogenic potentials in use include the post-auricular response and the trigemino-cervical reflex.[35]

Two types of VEMP are described based on the recording site. Cervical VEMP (cVEMP) is recorded from cervical muscles and Ocular VEMP (oVEMP) is recorded from the extraocular muscles.

Electrogenesis and physiological basis of cVEMP

The VEMP response normally consists of biphasic (positive and negative) waveforms (Fig -1). The crest and trough of the waveforms are labeled by lower case letters ("p" for positive and "n" for negative waves) followed by their mean latency in milliseconds. Four waves are seen including the first positive- negative wave complex called p13–n23 and the second wave complex called n34–p44. The second wave complex are inconsistent (absent in 40% of normal individuals), have a lower stimulus threshold and are probably cochlear in origin. [27,34]

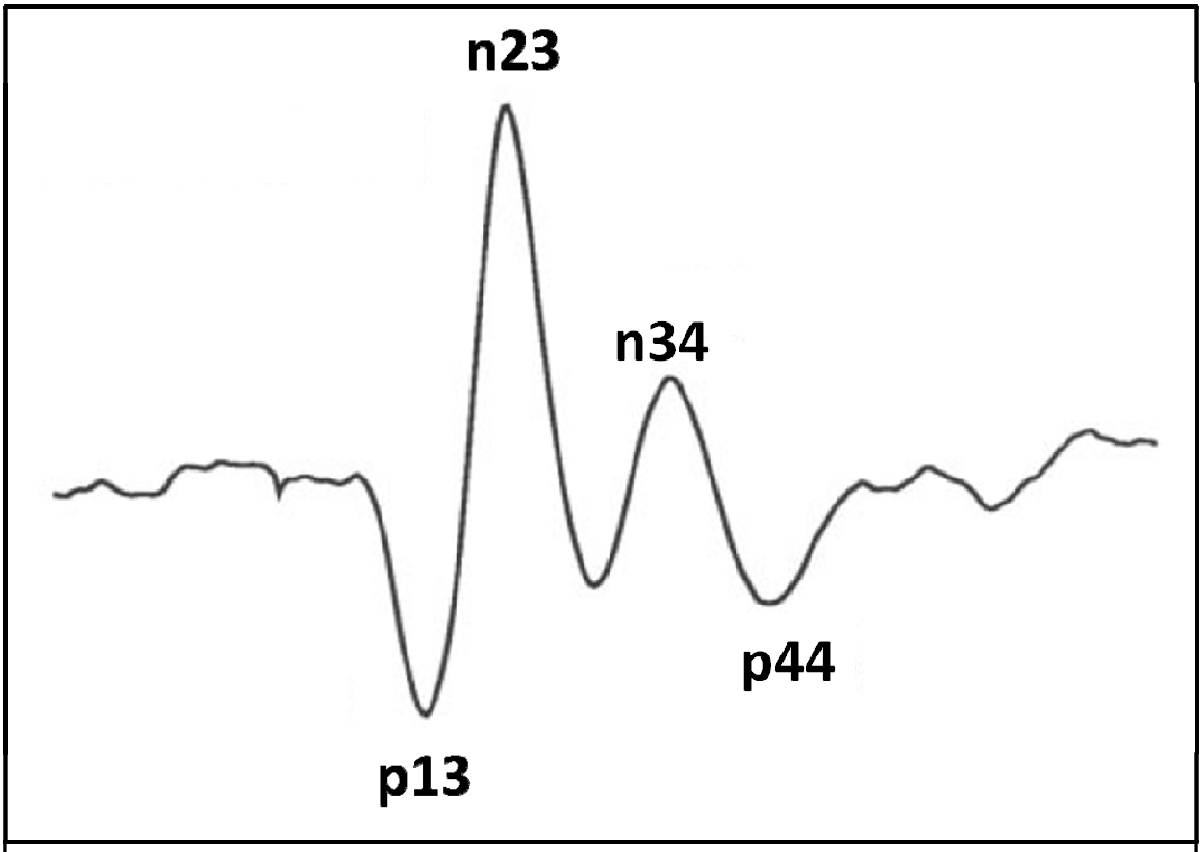

Fig - 1 : Normal Waveform of cervical VEMP

The positive wave of the cVEMP corresponds to a short period of inhibition in the sternocleidomastoid (SCM) and the negative wave to an excitation of SCM. The period of inhibition occurs between 8 and 20 milliseconds following the stimuli. The duration of inhibition is short and with auditory clicks, it ranges from 2 to 8 milliseconds with a mean of 3.6 milliseconds. The duration of inhibition or excitation increases in proportion to the intensity of the stimuli. VEMP response requires tonic contraction of the recorded muscle and it is due to an interruption

of activity and not due to summed synchronized neural action potentials as it occurs in evoked potentials.[36]

Neural pathway of cVEMP

cVEMP is the manifestation of vestibulo-collic reflex. This reflex has a short-onset latency of about 8 milliseconds. This indicates that cVEMP is likely to be mediated by an oligosynaptic pathway or disynaptic pathway. (Fig-2)

Receptor:

Saccule is the likely receptor for cVEMP as it is preserved in sensorineural hearing loss and semicircular canal ablation.

Afferent Pathways:

VEMP responses are mediated through the vestibular portion of the vestibulocochlear nerve. Anatomical evidence suggests that the impulse travels through the inferior vestibular nerve, which carries saccular afferents.

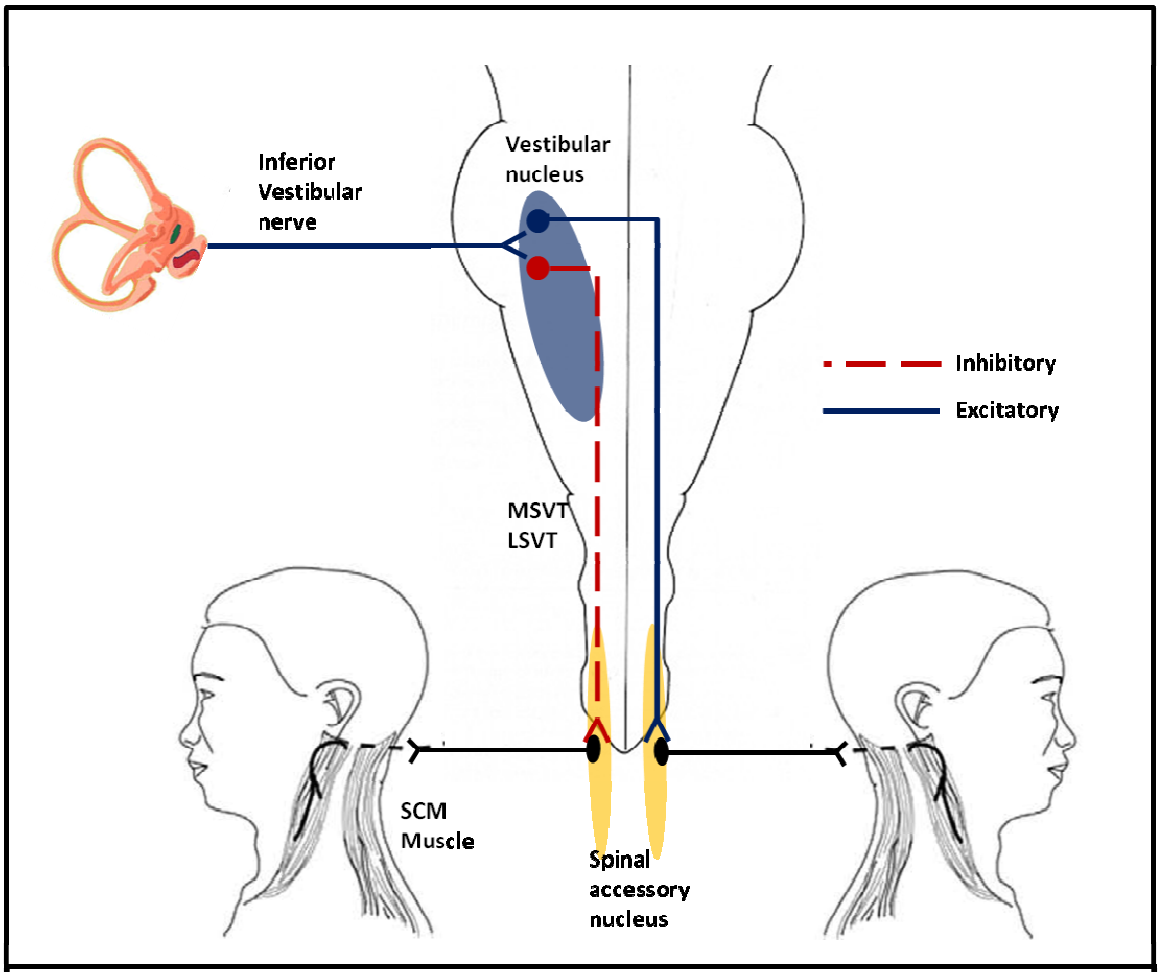

Fig - 2 : Neural pathway of Vestibulo-collic reflex

Center and Efferent Pathways:

Both medial vestibulospinal tract (MVST) and lateral vestibulospinal tract (LVST) acts as efferent pathways to sternocleidomastoid (SCM) from the Deiter's cells of the vestibular nucleus.

Different types of VEMP

Cervical VEMPs were initially evoked by auditory clicks but, they can also be elicited by other stimuli such as tone bursts, bone conducted vibration, head taps and galvanic vestibular stimulation.

Click and Tone evoked cervical VEMP

Stimulus characteristics

To evoke cVEMPs high intense clicks of around 95 to 100 decibels above the normal hearing level are required. This is equivalent to 140 to 145 decibel of sound pressure level (SPL) which is well tolerated and within the safe limits. In routine testing of VEMP, an accurately calibrated sound source is fundamental to deliver a stimulus of 0.1 millisecond (ms) duration at 95 decibels (db) normal hearing level (NHL).

An ideal amplifier setting for VEMP recording uses a gain of 5,000 (200 μV/V) with a band pass filter of 10 Hz to 2 kHz. Usually, 256 repetitions are averaged to obtain the response. A stimulus repetition rate of less than 5 Hz can be used without a decrease in the response amplitude.[37]

Alternate current tone burst cVEMPs have larger amplitude due to greater frequency tuning and stimulus duration than click cVEMPs (Fig -3). The VEMP amplitude increases with the intensity of click and tone-burst. However, the VEMP latency remains constant despite varying the intensity of the stimulus. The best frequency for AC tone burst is between 200 and 1000 Hz with largest tone burst evoked VEMPs to lowest thresholds obtained between the frequencies 500 and 750 Hz. The latency of VEMP is not dependent of stimulus frequency when duration of the tone-burst is held constant.[38]

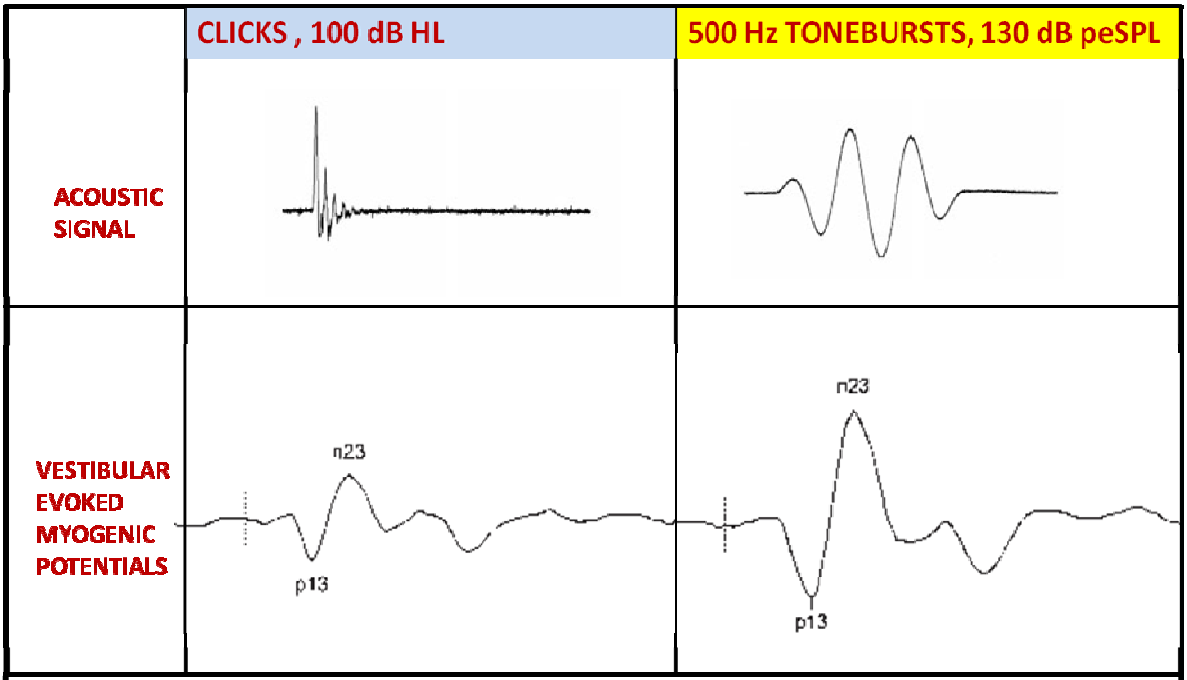

Fig - 3 : Comparison of click and tone burst evoked VEMPs

The middle ear conduction should be normal to transmit the impulse to the vestibular end organ. The VEMP response is attenuated or absent if, there is a

conductive hearing loss with air-bone gap more than 8.75 decibels.[39] If the subject has tinnitus click and tone burst VEMP are relatively contraindicated. However, in subjects with tinnitus, an alternate stimulus like head taps or galvanic electrical stimulation could be considered.

Stimulation mode

Monaural and binaural stimulation produces differences responses. There is no significant right to left difference in the amplitude with binaural stimulation. However, binaural stimulation produced larger amplitude response when compared to the monaural stimulation.[40] Bilateral stimulation is often considered a superior option in testing old or patients with disability.[41]

Effect of firing rate

The effect on the unrectified average EMG due to a change in the firing rate can be determined effectively using the convolution integral. The changes in the firing rate over a short period could account for certain characteristics of the vestibular evoked myogenic potentials. The resultant surface potential varies linearly with the increasing firing rate when evoked using a sine wave stimulus of 20

milliseconds duration, amplitude of 10µ volt and a sample rate of 5 kilo Hertz.

(Fig- 4)

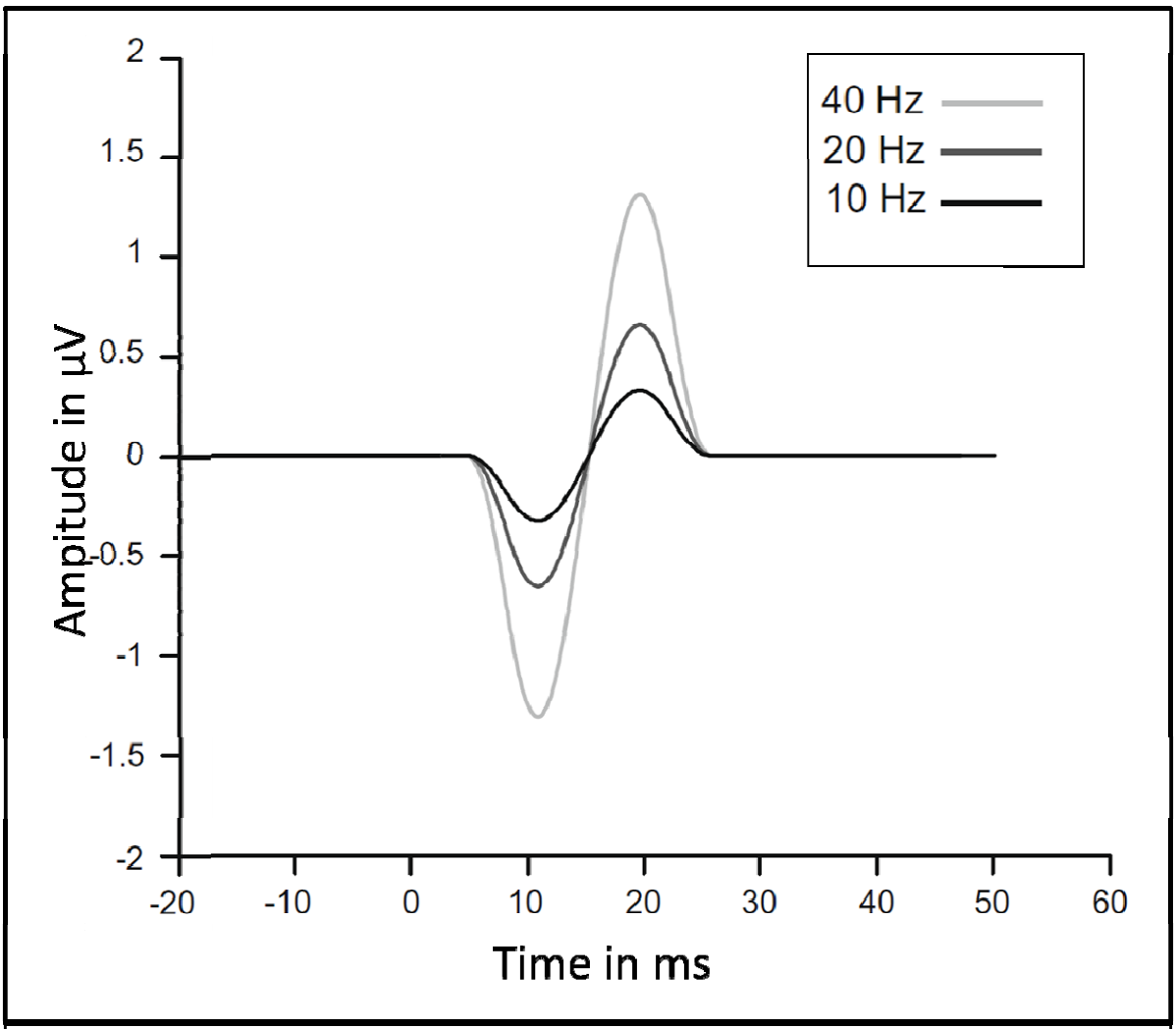

Fig- 4 : Effect of firing rate on VEMPs

The elicited surface myogenic response also varies linearly with the increasing duration of muscle inhibition when the firing rate is held constant. (Fig-5)

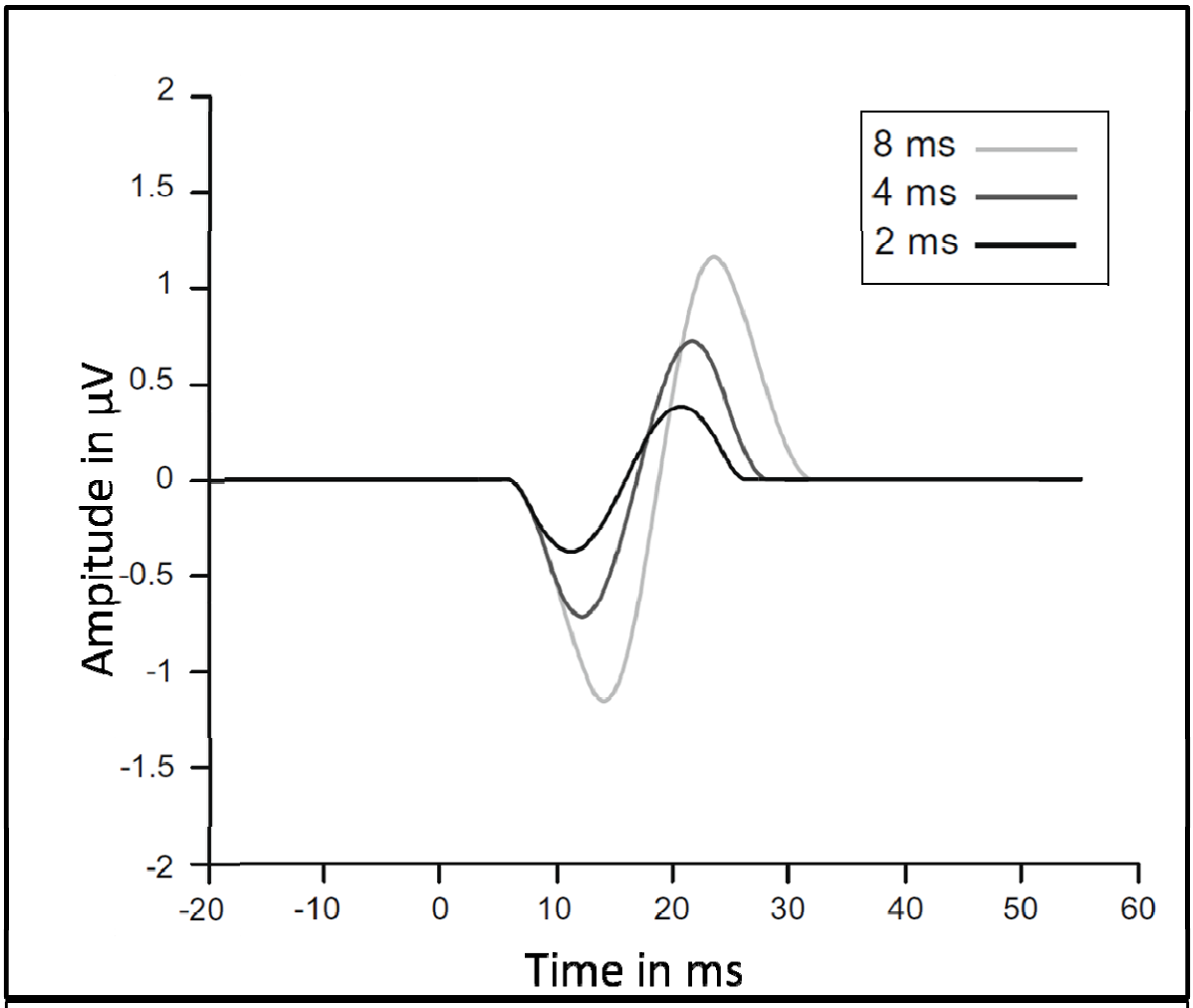

Fig- 5 : Effect of duration of inhibition on VEMPs

Thus, when the firing rate changes over longer duration the duration of the elicited myogenic response also increases with a proportional increase in the p13 and n23 peak latencies. This effect points that the amplitude affects the peak latencies.[29,42]

Recording site

Initial studies on VEMPs were done by placing the active electrode on inion. The inion responses showed symmetrical responses because of their midline location. Since Colebatch et al's revision of the recording procedure, sternocleidomastoid (SCM) muscles have become the preferred recording site.[43] Though VEMP recorded at the upper part of the sternocleidomastoid muscle has the larger amplitude of p13-n23, the ideal site for electrode placement is the middle third of the SCM where the latency of the first peaks (p13-n23) was consistent.[44]

A similar but bilateral VEMP response can also be recorded in response to acoustic stimuli over the tonically active trapezius, masseter and splenius capitis. In the masseter responses, the vestibular component could be clearly distinguished from the later occurring cochlear component.[45]

Response Laterality

The early studies on VEMP reported symmetric responses because of the midline position of the inion electrodes. However, with further refinements using sternocleidomastoid muscle as the standard recording site and mono aural stimuli the obtained responses are predominantly ipsilateral. The initial biphasic p13-

n23response is strictly ipsilateral to the stimulus and is vestibular dependent .[44] A crossed response of inverted polarity, with an initial negativity called the crossed neural response (n1-p1) may be present as well (fig -6). These crossed responses are usually small and becomes prominent in the presence of vestibular hypersensitivity to acoustic stimuli.[42]

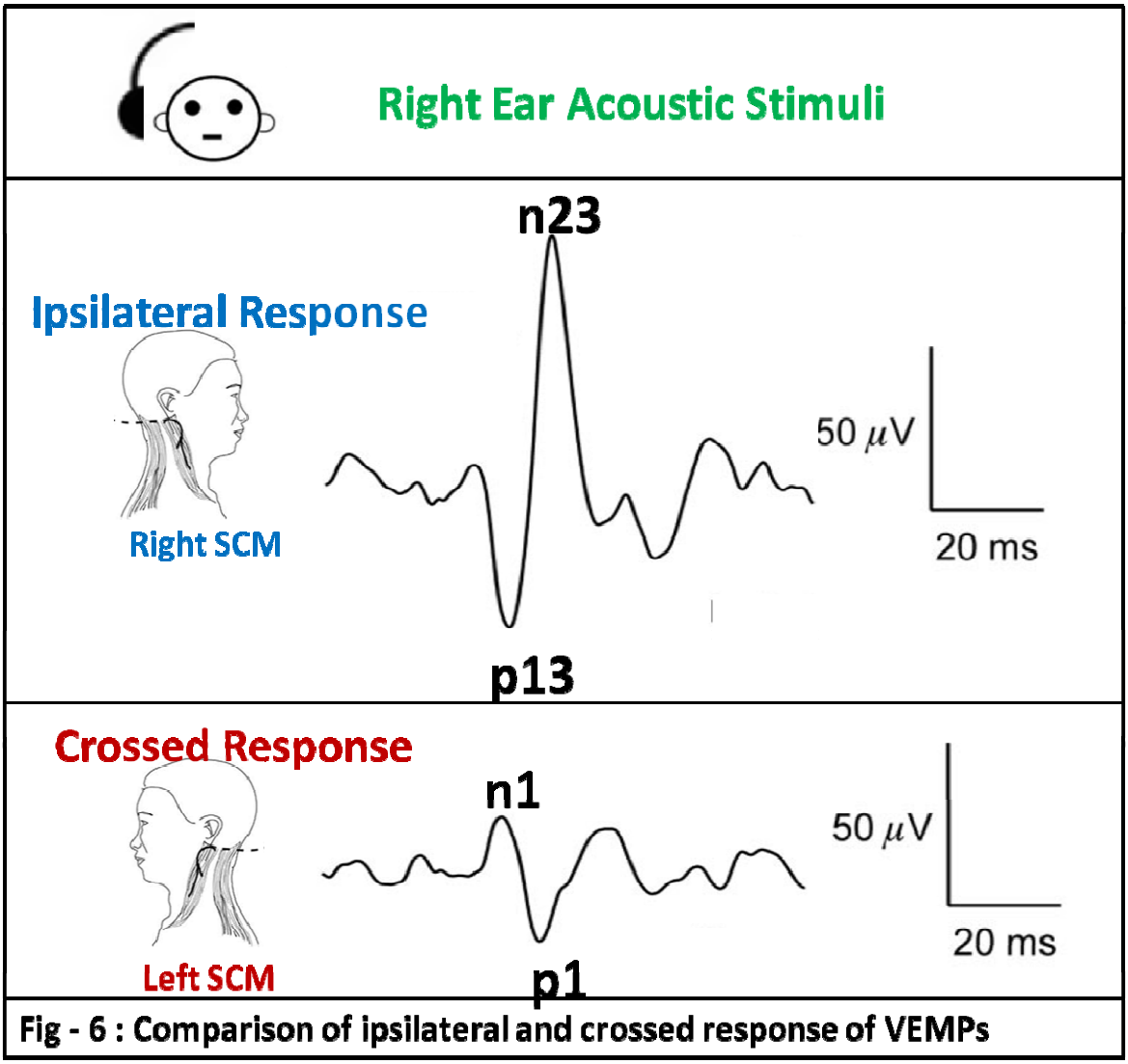

Fig - 6 : Comparison of ipsilateral and crossed response of VEMPs

Effect of muscle tension on VEMPs

Muscle tension significantly influences the VEMP responses. Muscle tension is linearly related to the amplitude of the VEMP response independent of the intensity of the stimuli. This has been quantified by mathematical analysis of the monitored electromyography activity with an oscilloscope.[24] An increase in muscle tension increases the amplitude of the response without affecting the latency of the response. The neck muscle can be activated by several maneuvers. This include

- Elevating the head from supine position.

- Turning the head away from the stimulated side in sitting position.

- Applying different loads to neck through a plastic loop and pulley.

- Pressing the head against a padded bar.

In activating the muscle, the muscle tension influences the response and not the head position.[46]

VEMP responses are best observed using averaged unrectified EMG. The vestibule-collic reflex amplitude rises in proportion to tonic activity of the EMG. Hence, the amplitude should be normalized to the level of pre stimulus EMG activity. (Fig- 7)

$$corrected\ Reflex\ Amplitude = \frac{Peak - Peak\ Amplitude}{prestimulus\ rectified\ EMG\ activity}$$

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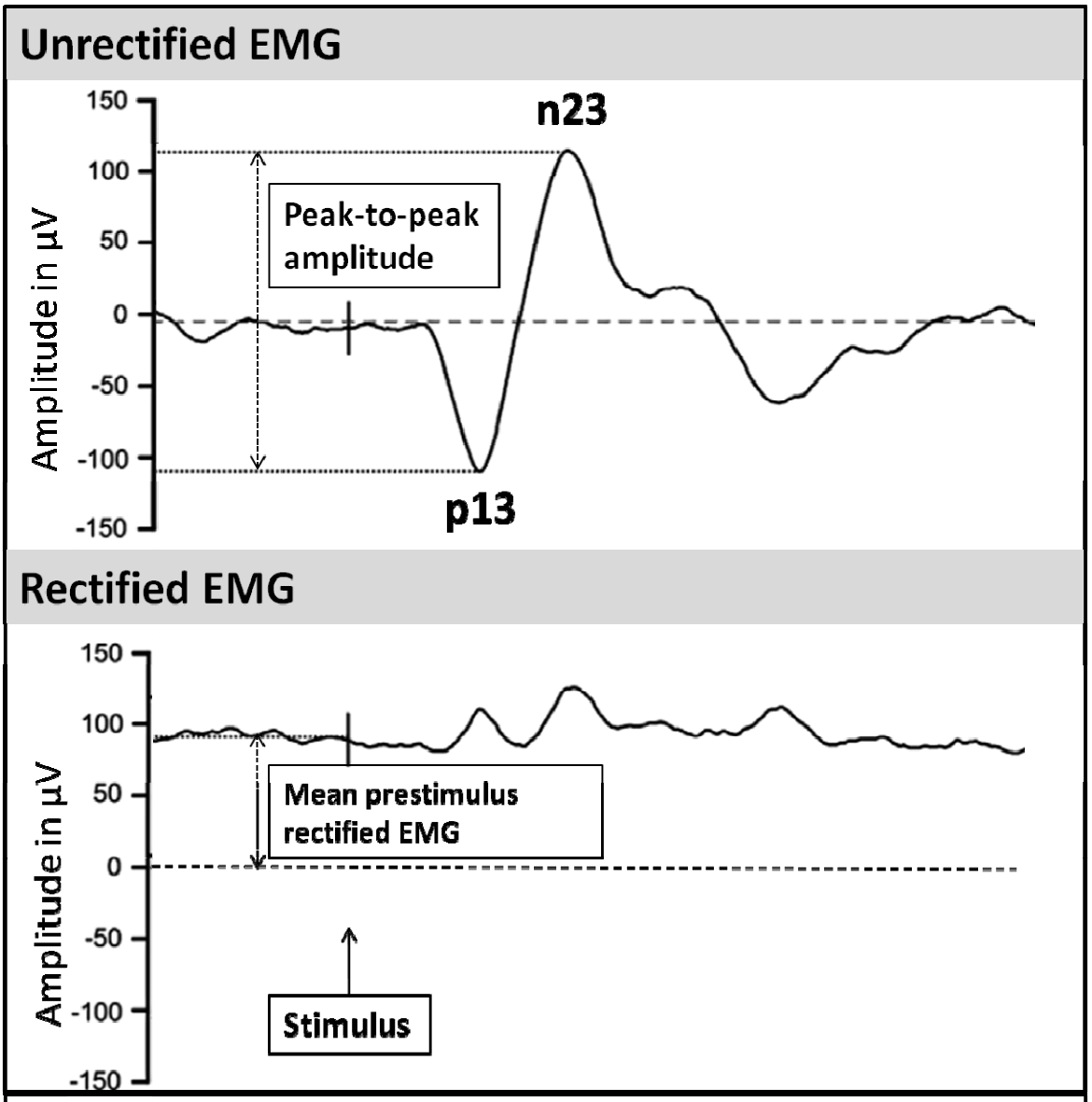


Fig - 7 : Rectified and unrectified EMG response of VEMPs

Cervical VEMP evoked by non-acoustic stimuli

Cervical VEMPs were initially evoked by auditory clicks but, they can also be elicited by other stimuli such as tone bursts, bone conducted vibration, head taps and galvanic vestibular stimulation.

VEMPs evoked by bone-conducted stimuli:

Stimulus like bone-conducted tones and skull taps bypass the conductive system in the middle ear and can evoke VEMP response even in the persons with conductive hearing loss.

Bone-conducted tones evoked VEMPs

VEMP response can be evoked by using a clinical bone vibrator to deliver a bone-conducted tone burst over the mastoid process. The preferred site of stimulation is 3cm posterior and 2cm superior to the external acoustic meatus. Optimum stimulation can be achieved by using atone burst frequencies of 200 to 250 Hz. The stimulus threshold for bone vibration is significantly lesser than the auditory stimuli. A stimulus threshold of less than 50 dB above hearing level strongly stimulates the vestibular end organ without the risk of cochlear injury.

As the stimulus is transmitted through bone, it activates vestibular end organs bilaterally and hence the VEMP response is often bilateral (Fig-8). However, the

ipsilateral VEMP response is around 1.5 times larger than the crossed response and it occurs about 1 ms earlier than the crossed response. Exceptionally larger VEMPs may be seen contralateral to the stimulated ear.[47]

Skull tap evoked VEMPs

A tendon hammer is used to deliver a forehead tap at the Fpz point as per the International 10–20 System can evoke a VEMP response. The recorded potential in both the sternocleidomastoid is a short-latency p1n1 response, which is vestibular dependent (Fig-8). A second negative (n2) may also be seen at times. A prominent crossed response is seen in unilateral vestibular diseases due to crossed excitation from the intact side. As the delivered skull taps are not calibrated this method is operator dependent. If the skull taps are delivered laterally superior to the ear inverted VEMPs is recorded in the in the ipsilateral SCM. Whereas, the contralateral SCM shows a response of normal polarity suggesting that the opposite vestibular apparatus is more effectively stimulated.[48]

Since the magnitude of the stimulus is larger compared to the click, skull tap-evoked VEMPs are also about 1.5 to 3 times larger than those evoked by clicks. They are more likely to be preserved in elderly subjects in whom stimulus thresholds are usually high.[28]

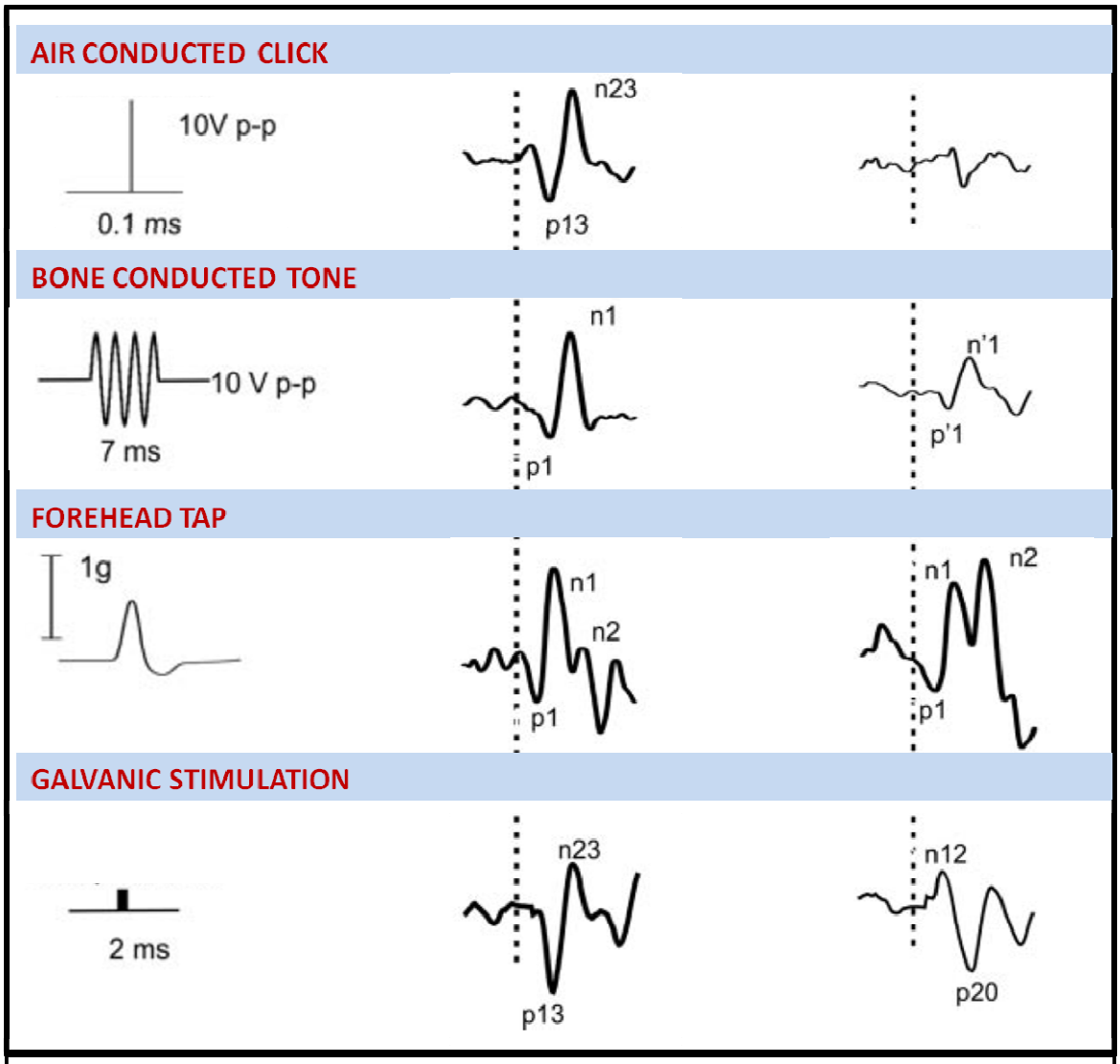


Fig - 8 : VEMPs evoked by different stimulus

VEMPs evoked by galvanic stimulation

A pulsed current of 2 millisecond duration delivered to an electrodes attached to the mastoid processes produces a VEMP response (p13n23) on the side of stimulation (Fig-8).[49] A low intensity Stimuli of around 4 mA over 2 ms is usually

suffice and is well tolerated. Anodal currents decrease and cathodal currents increase spontaneous firing rates. A monaural stimulus usually elicits a “p13n23” response ipsilaterally and a “n12p20” response contralaterally The crossed neural response is usually present in all the normal subjects indicating the activation of utricular afferents.[50] This feature helps in differentiating between labyrinthine (end organ) lesions and retrolabyrinthine (afferent) lesions since galvanic VEMPs are preserved in labyrinthine disease.[51]

Ocular VEMP

Extraocular electromyogram (EMG) activity that is related to vestibulo-ocular reflex can be studied by placing surface electrodes near the eyes. (Fig-9)

Bipolar montage with placement of the recording electrode close to the eye and the reference electrode 2–3 cm away is standard for recording ocular VEMP. The ocular VEMP tracing shows a series of biphasic waves. These waves begin with negativity with mean peak latency of around 10 ms called “n10 or n1”. Its negative polarity is due to underlying muscle activation whereas in cervical VEMPs it is due to inhibition of muscular activity.

Ocular VEMPs are evoked by either sound or vibrations and it is transmitted via the superior division of vestibular nerve.[29,36]

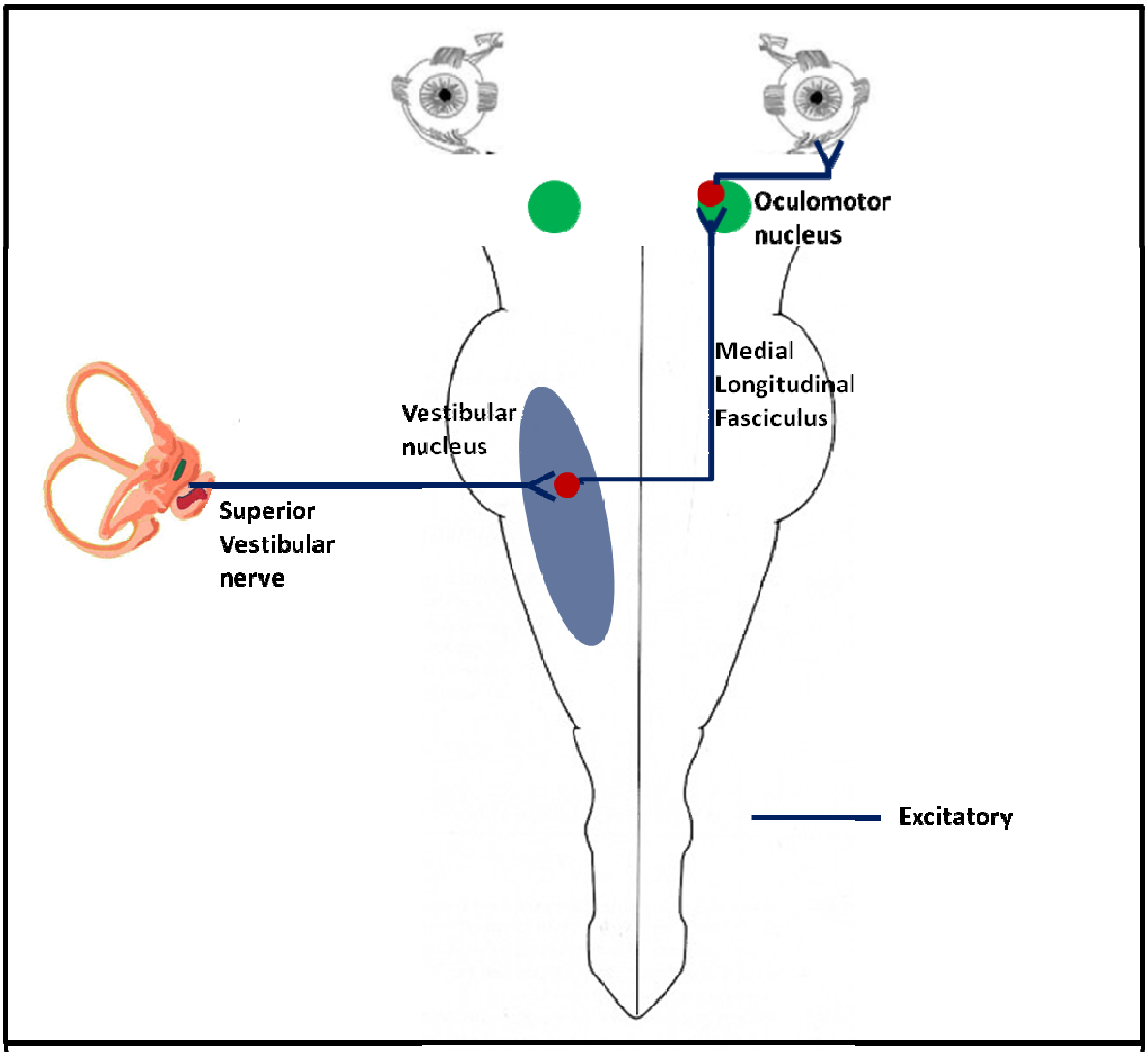


Fig - 9: Neural pathway of Vestibulo-ocular reflex

CLINICAL APPLICATION OF VEMP

Cervical VEMPs are obtainable in all normal individuals less than 60 years of age.

The amplitude of both the cervical and ocular VEMPs can be used as a

quantitative measure of otolith function. The amplitude of VEMPs decrease with age and are affected by peripheral vestibular disorders. The amplitude asymmetry ratio (AR) is calculated using the following formula is an important parameter.

$$AR = \{(Larger\ response - Smaller\ response) + (Larger\ response + Smaller\ response)\} \times 100$$

Threshold is studied by averaging the lowest intensity stimulus needed to evoke a response. The peak latency of VEMP responses should be recorded and are prolonged in central vestibulopathy. A larger amplitude VEMP response can lead to apparent latency prolongation.

The typically elicited threshold, amplitudes, asymmetry ratios, and latencies for cervical VEMP and ocular VEMP are tabulated (Table 5). Since these parameters are significantly influenced by stimulus modality, intensity and duration it is recommended that each institution should have their representative normative data.[29]

Table -5 : Reference values for cVEMP parameters					
STIMULUS	cVEMP				
	p13 (ms)	n23 (ms)	Corrected amplitude (μV)	Threshold (dB SPL/FL)	AR (%)
AC 0.1 ms click 145 dB SPL	12 ± 1.0	20.3 ± 1.7	1.22 ± 0.62 (0.5–3)	134.6 ± 6.9 (120–145)	<35
AC 5 ms/1 kHz tone 120 dB SPL			1.66	114.4 ± 4.4 (105–120)	<35.5
AC 6 ms/500 Hz tone 120 dB SPL	14.38 ± 0.19	24.9 ± 0.3	1.29 ± 0.15	110.25 ± 1.28 (105–120)	<62.7
BC tone at mastoid 136 dB FL	13.6 ± 1.8	22.3 ± 1.2	1.36 ± 0.45	126.1 ± 0.99 (122–136)	

VEMPs in central vestibulopathy

Prolongation of VEMP latency is the characteristic abnormality seen in central vestibular dysfunction.[52] Abnormalities in the VEMP response are present in medullary and mid to lower pontine lesions whereas BAER abnormalities are common in midbrain and pontine lesions. VEMPs are usually preserved in

midbrain and upper pontine lesions as the vestibular nuclei is below these structures.[53]

Subjects with multiple sclerosis have shown prolongation of p13 and n23 peak latencies. The abnormally prolonged latencies in multiple sclerosis were attributed to slowing of conduction in the vestibulospinal tracts due to demyelination. Peak latencies of p13 and n23 were significantly prolonged in the subgroup of patients with evidence of brainstem involvement. And the peak latencies also correlates well with the disease duration and disability scores.[54] VEMP responses may be absent in lateral medullary syndrome particularly in the acute stages.

VEMP in Parkinson's disease

Very few studies examined the vestibular myogenic potentials in central vestibular disorders. However abnormalities in the vestibular myogenic potentials were recorded in certain atypical parkinsonian syndromes such as olivopontocerebellar atrophy (OPCA) and progressive supranuclear palsy (PSP).[25,55]

A study examining the vestibular myogenic potential responses in idiopathic Parkinson's disease has shown increased frequency of absence of vestibule-collic reflex in PD patients compared to the control group.[56]

MATERIALS AND METHODS

Study Centre:

- ✓ Institute of Neurology, Madras Medical College and Rajiv Government General hospital,Chennai

Study design:

- ✓ Prospective case control study

Study period:

- ✓ January 2014 to March 2014 (3 months)

Study Sample:

- ✓ Thirty (30) patients with Parkinson disease and 30 healthy volunteers

Inclusion criteria:

- ✓ CASES: Patients with idiopathic Parkinson disease attending the Neurology services of Rajiv Gandhi Government General Hospital, Chennai.
- ✓ CONTROLS: Healthy attendants of the patients.

Exclusion criteria:

The patients with the following conditions were excluded from the study

- Parkinson plus syndrome
- Conductive hearing loss
- Tinnitus
- Patients on labyrinthine sedatives

Institutional ethical committee has approved the study. Informed consent were obtained from all the patients before the study.

Clinical Evaluation:

Clinical evaluations of all the patients were done with a proforma (see annexure) that includes the following.

- Demographic information
- Modified Hoehn and Yahr staging
- Unified Parkinson's disease Rating Scale (UPDRS)
- Tinetti balance assessment tool
- Drug history

Electrophysiological assessment

Standard methods for recording the auditory click evoked VEMP response are adapted.[24,28,57]

VEMP Recording

Subjects were examined in recumbent position with their trunks around 30^0 to 45^0 from the horizontal plane. Sternocleidomastoid (SCM) was activated by asking the subjects to lift their head against gravity. Surface electromyogram (EMG) was recorded by placing the active electrode the middle of the Sternocleidomastoid (SCM) muscle. The reference electrode is placed over the medial end of the clavicle. The ground electrode is applied to the sternum. Electromyogram (EMG) was sampled at 5 kHz from 20 ms before to 100 ms after the stimulus onset. The electromyogram (EMG) was amplified, filtered (10—500 Hz) and averaged appropriately. Unrectified electromyogram (EMG) averages were used to measure reflex latencies.

VEMP Stimulus

Brief high intensity rarefaction click stimuli were delivered separately to each ear via the headphones. Stimulus is started at an intensity of 60 decibel hearing level (dBHL) and rising by 10-dB steps till 110 dBHL. Stimulation rate was set at 3 Hz and analysis time was 100ms duration. Averaged responses to 128 stimuli were recorded. The procedure was done at least twice to ensure reproducibility (Medelec Premiere EMG System).

P13 latencies were measured from stimulus onset to peak of the initial positivity and n23 latencies to the next negativity. The latencies were assessed ipsilateral to the stimulated ear.

RESULTS AND OBSERVATIONS

CHARACTERISTICS OF PATIENT AND CONTROL

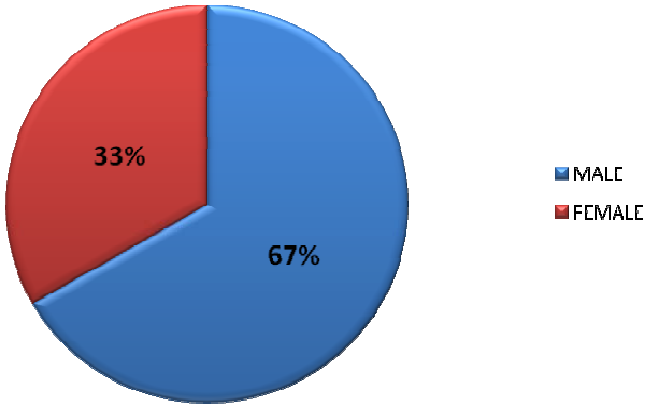
SEX DISTRIBUTION

Table - 6 : Sex distribution in PD patients

SEX	NUMBER	FREQUENCY
MALE	20	67%
FEMALE	10	33%
Total	30	100%

Thirty patients with Parkinson's disease were included in this study. Male patients were more common accounting for 67% (n=20). Female patients formed the rest 33 %(n=10).

Graph – 1: Sex distribution in PD patients



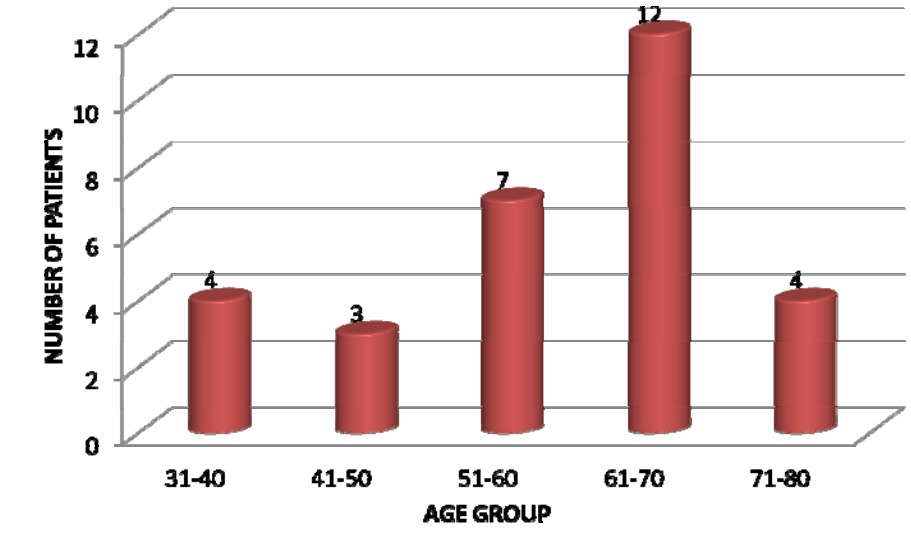
AGE DISTRIBUTION

Table - 7 : Age distribution in PD patients

AGE GROUP	NUMBER OF PATIENTS	FREQUENCY
31-40	4	13%
41-50	3	10%
51-60	7	23%
61-70	12	40%
71-80	4	13%
TOTAL	30	100%

The majority of patients with PD were from 61 to 70 years (40% / n=12). Patients from the age group 41 to 50 years were the least 10% / n=3).

Graph -2 : Age distribution in PD patients

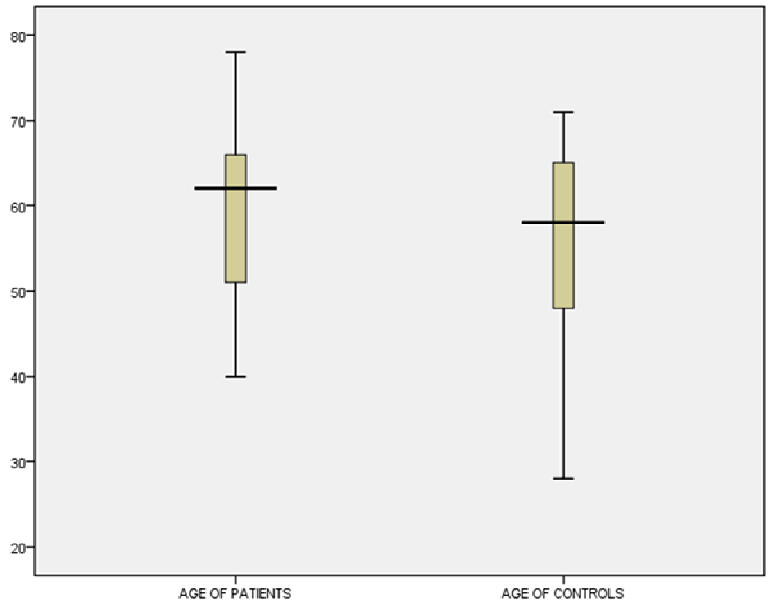


COMPARISON OF AGE DISTRIBUTION OF PD PATIENTS & CONTROLS

Table - 8 : Comparison of age distribution of PD patients & controls		
	AGE OF PATIENTS	AGE OF CONTROLS
N	30	30
Mean	58.87	56.10
Median	62.00	58.00
Minimum	40	28
Maximum	78	71
Range	38	43
Std. Deviation	10.903	10.417
Skewness	-.384	-.722
Kurtosis	-.638	.270

Age distribution of the patient and control group was matched with a mean of 58.87 in patients and 56.10 in the controls. The age is normally distributed as suggested by a smaller skew and kurtosis.

Graph - 3 : Box plot of age distribution of PD patients & controls



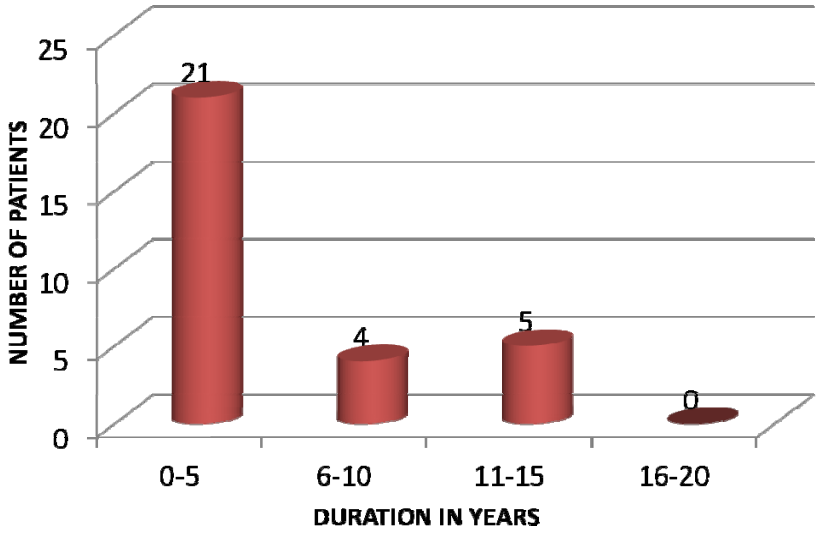
DURATION OF PARKINSON'S DISEASE

Table - 9 : Distribution of the duration of disease

DURATION OF PD	NUMBER OF PATIENTS	FREQUENCY
0-5	21	70%
6-10	4	13%
11-15	5	17%
16-20	0	0%
TOTAL	30	100%

Majority of the patients in this study had the disease for less than 5 years duration (70% / n=21). The remaining patients had the duration of the disease between 6 and 15 years.

Graph - 4 : Distribution of the duration of disease



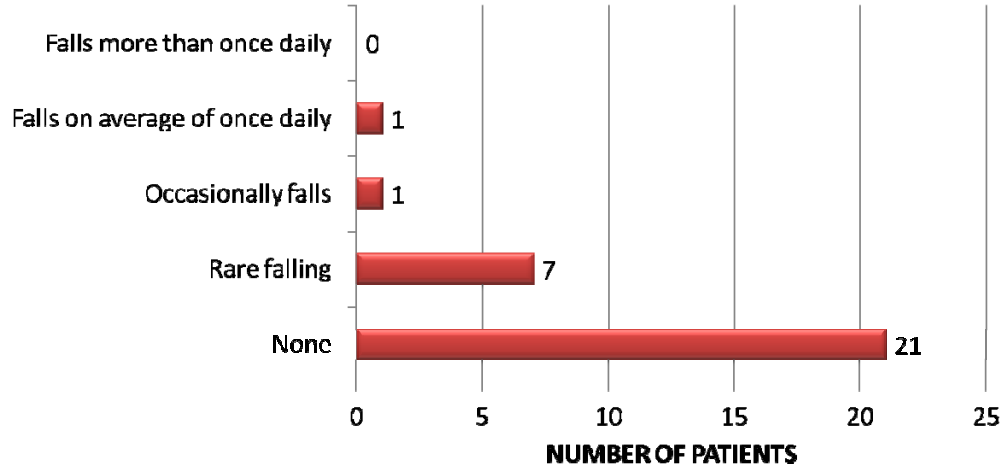
HISTORY OF FALLS IN PATIENTS

Table - 10 : Distribution of falls in patients

FALLS	NUMBER OF PATIENTS	FREQUENCY
None	21	70%
Rare falling	7	23%
Occasionally falls	1	3%
Falls on average of once daily	1	3%
Falls more than once daily	0	0%
TOTAL	30	100%

Thirty percent (n=9) of the patients with Parkinson's disease reported falls. Of them 23% (n=7) sustained only rare falls. Whereas daily falls was reported by only one patient.

Graph - 5 : Distribution of falls in patients



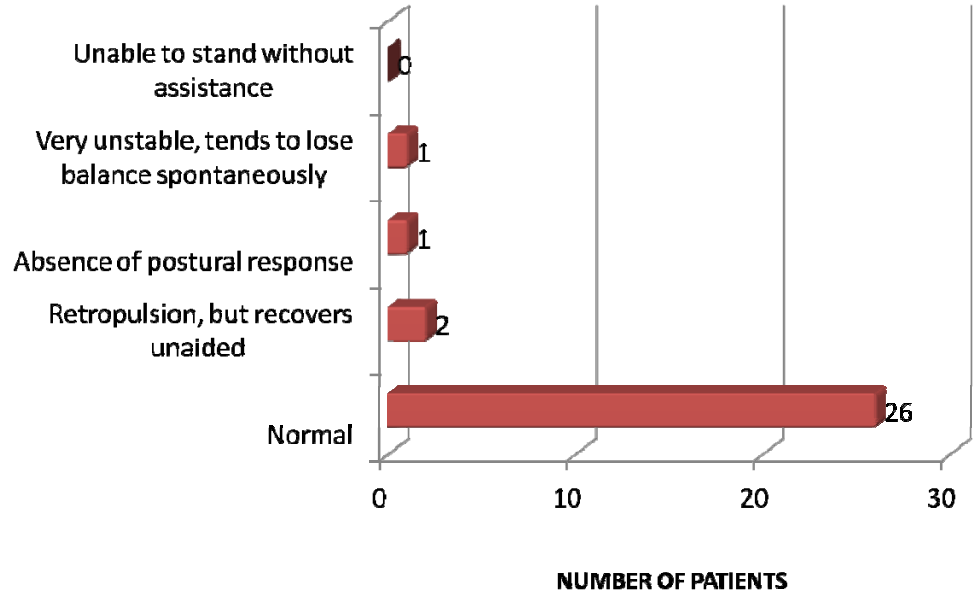
POSTURAL INSTABILITY – PULL TEST

Table - 11 : Distribution of postural instability by pull test in patients

POSTURAL INSTABILITY	NO OF PATIENTS	FREQUENCY
Normal	26	87%
Retropulsion, but recovers unaided	2	7%
Absence of postural response	1	3%
Very unstable, tends to lose balance spontaneously	1	3%
Unable to stand without assistance	0	0%
TOTAL	30	100%

Four patients (13%) demonstrated abnormalities in the pull test for postural instability. Retropulsion test were normal in the rest of 26 patients (87%).

Graph - 6 : Distribution of postural instability by pull test in patients



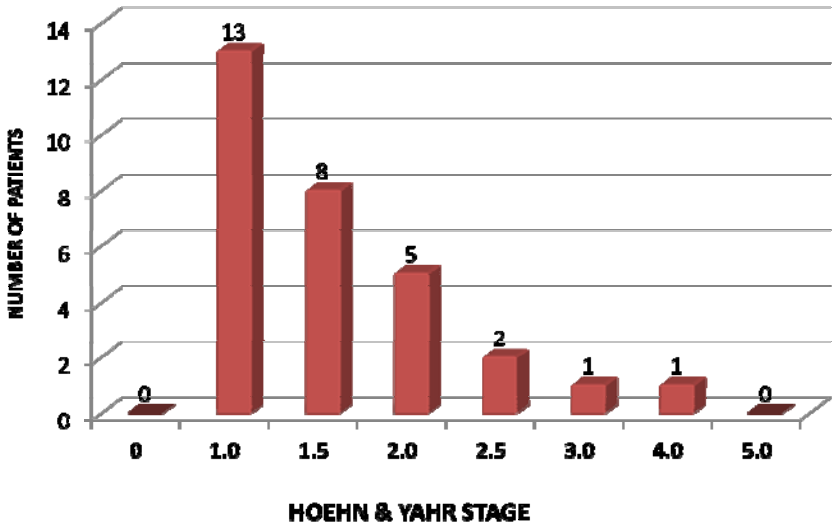
HOEHN AND YAHR STAGING

Table - 12 : Distribution of Hoehn & Yahr stages in patients

HOEHN & YAHR STAGE	NUMBER OF PATIENTS	FREQUENCY
0	0	0%
1.0	**13**	**43%**
1.5	8	27%
2.0	**5**	**17%**
2.5	2	7%
3.0	**1**	**3%**
4.0	1	3%
5.0	**0**	**0%**
TOTAL	30	100%

Majority (43% / n=13) of the studied patient had stage 1 disease. None of the patients had stage 5 disease.

Graph - 7 : Distribution of Hoehn & Yahr stages in patients



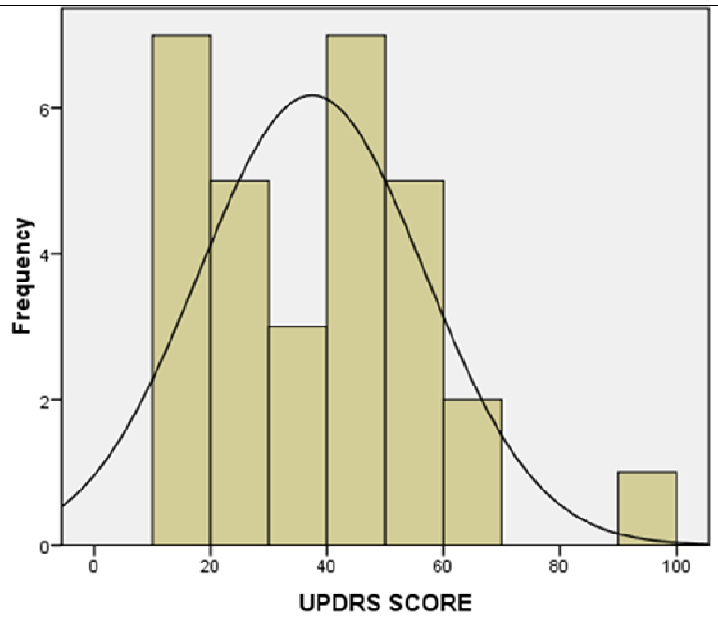
UPDRS SCORES OF THE PATIENTS

Table - 13 : UPDRS scores of the patients

Parameter		Value
N	Valid	30
	Missing	0
Mean		37.43
Median		39.50
Std. Deviation		19.378
Skewness		.651
Std. Error of Skewness		.427
Kurtosis		.387
Std. Error of Kurtosis		.833
Range		81
Minimum		10
Maximum		91

The mean UPDRS score was 39.5 ranging from 10 to 81. The skew and kurtosis of the scores were low suggesting a normal distribution.

Graph - 8 : Frequency histogram of UPDRS scores of the patients

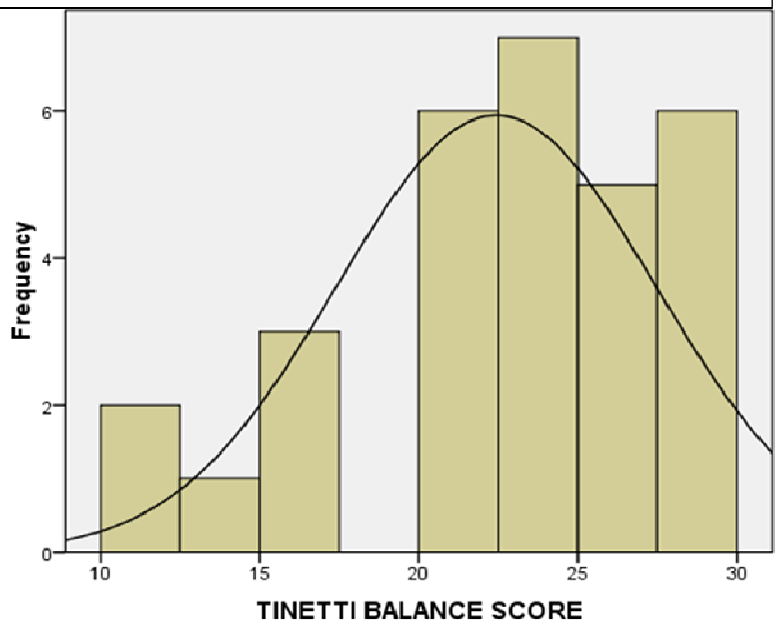


TINETTI SCORE and RISK OF FALL

Table - 14 : Tinetti score of the patients		
Parameter		Value
N	Valid	30
	Missing	0
Mean		22.43
Median		23.00
Std. Deviation		5.036
Skewness		-.961
Std. Error of Skewness		.427
Kurtosis		.388
Std. Error of Kurtosis		.833
Range		18
Minimum		10
Maximum		28

The mean Tinetti score was 22.43 ranging from 10 to 28. The skew and kurtosis of the scores were low suggesting a normal distribution.

Graph - 9 : Frequency histogram of Tinetti score of the patients



VESTIBULAR EVOKED MYOGENIC POTENTIALS (VEMP)

The following figures shows normal and absent VEMPs (Fig-10 & 11)

Fig - 10 : Normal VEMP recording

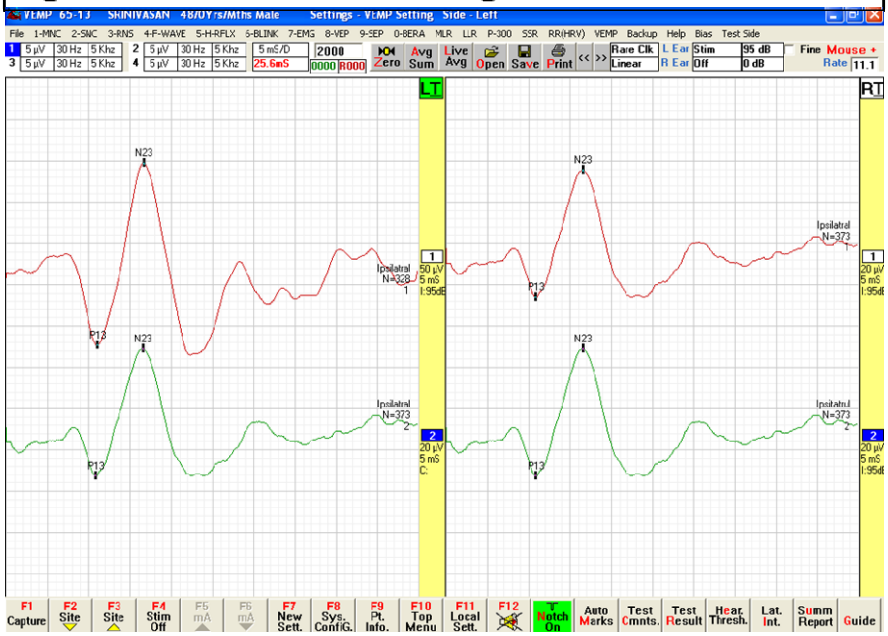


Fig - 11 : Absent VEMP recording

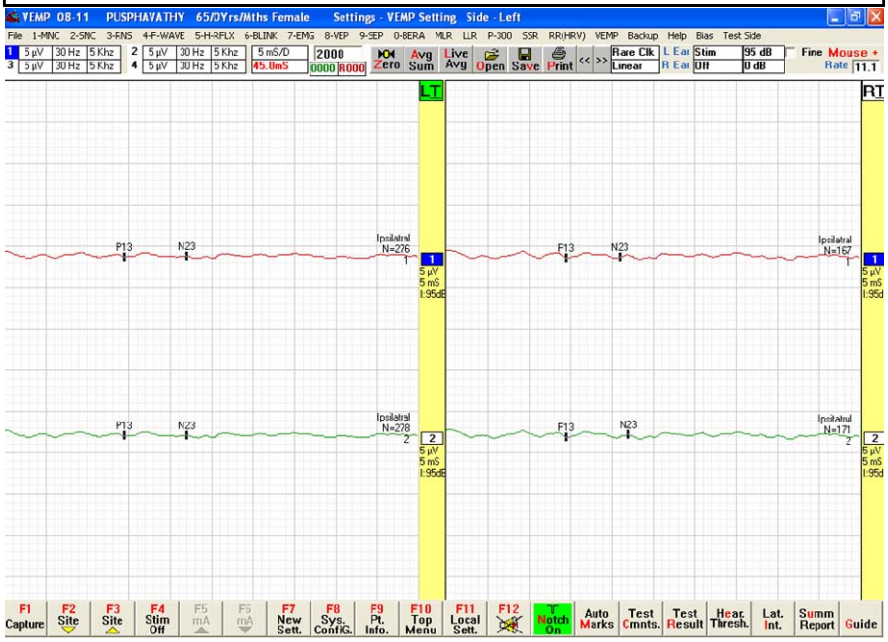
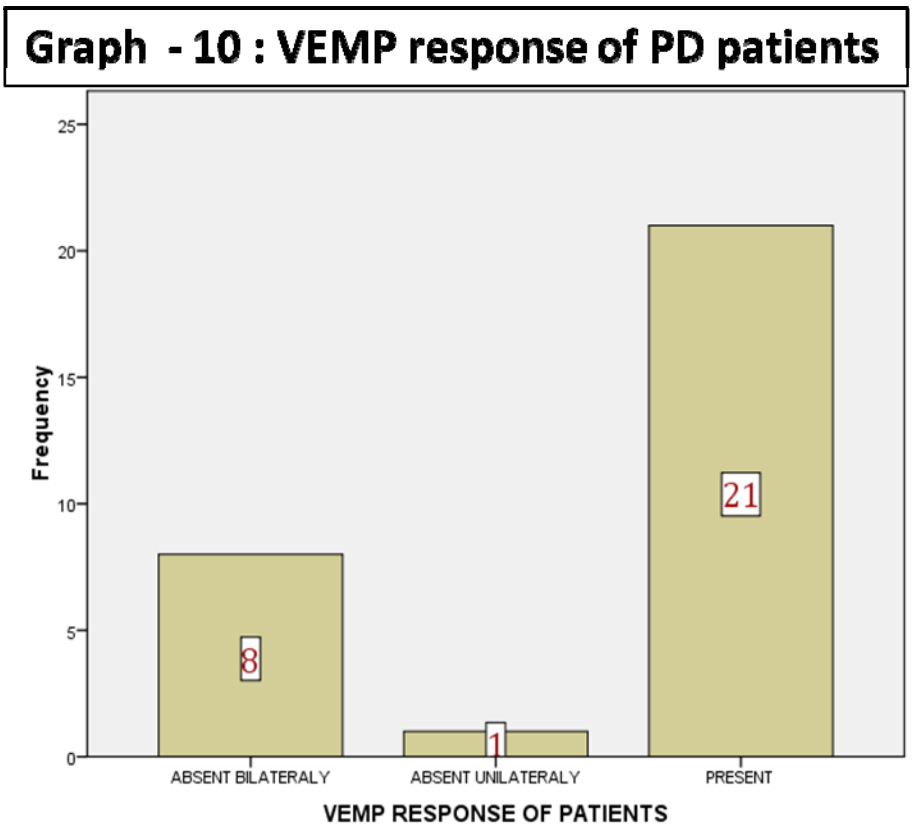


Table - 15 : VEMP response of PD patients			
	Frequency	Percent	Cumulative Percent
ABSENT BILATERALY	8	26.7	26.7
ABSENT UNILATERALY	1	3.3	30.0
PRESENT	21	70.0	100.0
Total	30	100.0	

The VEMP responses are obtained in all controls whereas it is bilaterally absent 8 patients (2.7%) with PD patients unilaterally absent in 1 (3.3%) patient.



COMPARISON OF VEMP RESPONSE WITH AGE

Table - 16 : VEMP response and age				
		AGE OF THE PATIENT		Total
		< 60 YEARS	> 60 YEARS	
VEMP RESPONSE OF PATIENTS	PRESENT	9	12	21
	ABSENT	5	4	9
	Total	14	16	30

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	.408[a]	1	.523

The VEMP responses of the patients with Parkinson's disease is not affected by the age of the patient ($p>0.05$).

COMPARISON OF VEMP RESPONSE WITH HISTORY OF FALLS

Table - 17 : VEMP response of patients and history of falls				
		HISTORY OF FALLS		Total
		PRESENT	ABSENT	
VEMP RESPONSE OF PATIENTS	PRESENT	4	17	21
	ABSENT	5	4	9
	Total	9	21	30

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	3.998[a]	1	.046

The difference in the VEMP responses between the patients with fall and the patients without fall is statistically significant (p=0.046).

COMPARISON OF VEMP RESPONSE WITH POSTURAL INSTABILITY

Table - 18 : VEMP response and postural instability

		POSTURAL INSTABILITY		Total
		PRESENT	ABSENT	
VEMP RESPONSE OF PATIENTS	PRESENT	1	20	21
	ABSENT	3	6	9
Total		4	26	30

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	4.451[a]	1	.035

The difference in the VEMP responses between the patients with postural instability and the patients without postural instability is statistically significant (p=0.035).

COMPARISON OF VEMP RESPONSE WITH HOEHN & YAHR STAGE

The variation of VEMP response with different Hoehn and Yahr staging was not found to be significant (p=0.052).

Table - 19 : VEMP response of patients and Hoehn & Yahr stage

		HOEHN & YAHR STAGE						Total
		H & Y STAGE 1	H & Y STAGE 1.5	H & Y STAGE 2.0	H & Y STAGE 2.5	H & Y STAGE 3.0	H & Y STAGE 4.0	
VEMP RESPONSE OF PATIENTS	PRESENT	12	5	3	0	0	1	21
	ABSENT	1	3	2	2	1	0	9
Total		13	8	5	2	1	1	30

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	10.962[a]	5	.052

COMPARISON OF VEMP RESPONSE WITH UPDRS AND TINETTI SCORE

Table - 20 : Analysis of variance (ANOVA)

	Sum of Squares	df	Mean Square	F	Sig.
UPDRS SCORE And VEMP RESPONSE	1687.240	1	1687.240	5.134	.031
TINETTI SCORE And VEMP RESPONSE	90.668	1	90.668	3.938	.057

The variation of the VEMP responses with the UPDRS score was found to be significant (p=0.031). Whereas the variation of the Tinetti balance tool score was not significant (p=0.057).

COMPARISON OF P13 AND N23 LATENCIES OF PD PATIENTS AND CONTROLS

Table - 21 : Comparison of p13 and n13 latencies of PD patients & controls

	N	Range	Minimum	Maximum	Mean	Std. Deviation
p13 LATENCY OF PD PATIENTS	43	5.0	9.2	14.2	**12.258**	1.1119
n 23 LATENCY OF PD PATIENTS	43	6.9	15.1	22.0	**20.056**	2.0585
p13 LATENCY OF CONTROLS	60	5.4	9.2	14.6	**12.337**	1.2032
n 23 LATENCY OF CONTROLS	60	9.2	13.2	22.4	**19.925**	2.3052

The p13 and n23 latencies of the PD patients and controls are given in the table above. The mean of p13 latency of the patients is 12.26 and that of the controls is 12.36. The mean n23 latency of the patients is 20.06 and that of the controls is 19.93.

Table - 22 : Analysis of variance (ANOVA)					
	Sum of Squares	df	Mean Square	F	Sig.
P13 LATENCY OF PD And P13 LATENCY OF CONTROLS	20.467	15	1.364	1.829	.235
N23 LATENCY OF PD And P13 LATENCY OF CONTROLS	62.915	15	4.194	.879	.612

P13 latency of the patients with Parkinson's disease did not differ from that of the controls (p=0.235). N23 latencies of the patient group also did not differ from the control group (p-0.612).

COMPARISON OF UPDRS SCORE WITH FALLS & POSTURAL INSTABILITY

Table - 23 : Analysis of variance (ANOVA)					
	Sum of Squares	df	Mean Square	F	Sig.
UPDRS SCORE And HISTORY OF FALLS	5205.906	1	5205.906	25.647	.001
UPDRS SCORE And POSTURAL INSTABILITY	3319.078	1	3319.078	12.276	.002

The higher UPDRS scores were significantly associated with the risk of fall and postural instability on pull test (p= 0.001 & 0.002).

COMPARISON OF TINETTI SCORE WITH FALLS & POSTURAL INSTABILITY

The higher Tinetti scores were significantly associated with the risk of fall and postural instability on pull test (p= 0.001 & 0.001).

Table - 24 : Analysis of variance (ANOVA)

	Sum of Squares	df	Mean Square	F	Sig.
TINETTI SCORE And HISTORY OF FALLS	349.144	1	349.144	25.312	.001
TINETTI SCORE And POSTURAL INSTABILITY	432.771	1	432.771	40.045	.001

COMPARISON OF UPDRS SCORE WITH TINETTI SCORE

Table - 25 : Comparison of UPDRS and Tinetti score			
	Mean	Std. Deviation	N
UPDRS SCORE	37.43	19.378	30
TINETTI BALANCE SCORE	22.43	5.036	30

Correlations

		TINETTI BALANCE SCORE	Sig. (2-tailed)
UPDRS SCORE	Pearson Correlation	-.837	.001

Higher UPDRS scores were significantly correlated with the lower Tinetti balance tool scores (p=0.001 / r= -0.837).

DISCUSSION

Falls and disorders of balance in patients with Parkinson's disease are attributable to many factors. These include abnormal motor processing, defective central processing of visual, vestibular or proprioceptive stimuli and impaired sensorimotor integration. [58,59]

The exact contribution of vestibular dysfunction to dysequilibrium and postural instability in patients with PD remains uncertain. Studies analyzing the different

parts of the vestibular system for their role in postural instability in PD have come up with mixed results.

Tests that specifically assess the lateral semicircular canals and their connections (rotational chair test and caloric test) were shown to be abnormal in PD. However further studies have demonstrated that this finding to be inconsistent.[19–21]

Studies testing the tilting table to examine the postural reflexes (an otolith reaction) showed abnormalities during the tonic phase. However, it remains to be proven that tilting table response specifically assesses the otolith function.[22]

Galvanic stimulation of the vestibular nerve (activates utricular part of vestibulospinal reflex) did not show any differences in postural sway between patients with PD and the controls.[23]

Vestibular myogenic potentials (VEMP) evoked by auditory clicks is a recently added tool in the assessment of otolith function.[24–28]

Vestibular myogenic potentials are shown to assess the sacculospinal (vestibulo-collic) reflex pathways including its afferent in the inferior division of vestibular nerve; centre in pons and medulla; efferent in the vestibulospinal pathways.[33,43]

Vestibulo-collic reflex is not considered a major element of the postural reflexes. However, VCRs have been shown to play an active part in movement of head in the sagittal plane (pitch movement) more during the passive head movements than active one. Thus vestibulo-collic reflex helps in stabilization of gaze and head position with respect to the gravitational coordinates. These functions of VCR serve to fix the gaze and head during the perturbations occurring in the process of the gait cycle.[60,61]

In our study we have found that click evoked VEMP responses were absent in 30% (n=9) of the patients with Parkinson's disease. Most of them had bilateral absence in the VEMP responses (bilateral Vs unilateral = 26.7% Vs 3.3%). Whereas all the controls (n=30) had normally obtainable VEMPs. This finding could not be attributed to the age as the age group of patient and control is matched (Table-8 and Graph-3). Moreover within the patients group the presence or absence of VEMP responses is not related to the age (Table-16).

In a recent study patients with Parkinson's disease were reported to have absence in the VEMPs. [56] However this study has found that the absent VEMPs are most often unilateral.

VEMP responses should be obtainable in all normal individuals.[28] Impairment in the vestibulo-collic reflex has been reported in Progressive supranuclear palsy, which is one of the Parkinson plus syndromes. [25] This study has demonstrated significant decrement in the amplitude of the VEMP response with preserved peak latencies. This defect in the saccular mediated vestibulo-collic reflex has been partly attributed to the falls in Progressive supranuclear palsy.

We have not measured the amplitude of the VEMPs in our study. The amplitude of the VEMP responses is significantly dependent on the activation of neck muscles which cannot be achieved without adequate cooperation from the patient and accurate measures to quantify the baseline activation of the neck muscles.[43,57] Hence we omitted the amplitude measurement in our study.

Absent VEMP responses were significantly related to the reported falls and the abnormal postural instability as tested by the pull (retropulsion) test (Table- 17 & 18). However the absent VEMO responses did not correlate significantly with the Hoehn and Yahr staging of the disease (Table- 19).

The p13 and n23 latencies of the obtained VEMPs of the patients with Parkinson's disease did not significantly differ from that of the controls (Table-21 & 22).

We have also found significant correlation between the UPDRS score and Tinetti score (Table- 25).

Our study shows a significant correlation of UPDRS score with the falls and postural instability (Table- 23). And Tinetti score also correlated significantly with the falls and postural instability (Table- 24). This is in agreement with the previous studies.[13,62–64]

The limitations of our study include insufficient enrolment of patients with advanced stages of the disease and lack of measurement of the amplitude of VEMPs.

CONCLUSION

The abnormalities in the vestibular system particularly of the otolith component could contribute to the disequilibrium in patients with Parkinson's disease.

Based on our observations and analysis we conclude,

- Auditory click evoked cervical VEMPs has a significant role in the assessment of vestibular function in patients with Parkinson's disease.
- Bilaterally absent VEMPs are a pointer to the otolithic vestibular dysfunction in patients with Parkinson's disease.
- Peak latencies of the p13 and n23 are not prolonged in patients with Parkinson's disease.
- VEMPs in patients with Parkinson's disease seem to follow an "all or none" response either with a present or absent response.
- Cervical VEMPs in patients with Parkinson's disease correlate significantly with falls and postural instability.
- Cervical VEMPs may serve as a predictor or marker of falls and postural instability in patients with Parkinson's disease.

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ABBREVIATIONS

VEMP - Vestibular evoked Myogenic Potentials

cVEMP - Cervical Vestibular evoked Myogenic Potentials

oVEMP - Ocular Vestibular evoked Myogenic Potentials

SNHL - Sensorineural Hearing Loss

PD - Parkinson's Disease

IPD - Idiopathic Parkinson's Disease

UPDRS - Unified Parkinson's disease Rating Scale

SPES - Short Parkinson's Evaluation Scale

SCOPA - Scale for Outcomes in Parkinson's disease

THESIS- PROFORMA

Min no		Name	
Age		Sex	
Duration of PD		Hoehn & Yahr stage	

UPDRS SCORE			
1.Mentation		22. Rigidity	
2. Thought disorder		23. Finger taps	
3. Depression		24. Hand grips	
4. Motivation/initiative		25. Hand	
5. Speech		27. Arise from chair	
6. Salivation		28. Posture	
7 . Swallowing		29. Gait	
8 . Handwriting		30. Postural stability	
9 . Cutting food		31. Body bradykinesia	
10. Dressing		32. Dyskinesia (duration)	
11 . Hygiene		33. Dyskinesia (disability)	
12. Turning in bed		34. Dyskinesia (pain)	
13. Falling		35. Early morning dystonia	
14. Freezing		36. “offs” (predictable)	
15. Walking		37. “offs” (unpredictable)	
16. Tremor		38. “offs” (sudden)	
17 . Sensory symptoms		39. “offs” (duration)	
18 speech		40. Anorexia, nausea, vomiting	
19 . Facial expression		41. Sleep disturbance	
20. Tremor at rest		42. Symptomatic orthostasis	
21. Action tremor		Total score	

Tinetti balance assessment tool			
Indication of gait		Sitting Balance	
Step length and height		Rises from chair	
Foot clearance		Attempts to rise	
Step symmetry		Immediate standing Balance	
Step continuity		Standing balance	

Path		Nudged			
Trunk		Eyes closed			
Walking stance		Turning 360 degrees			
		Sitting down			
Drugs		Total score			
Syndopa		Anticholinergics		Antidepressant	
Dopamine-agonists		COMT-inhibitor		Neuroleptics	
VEMP					
Right	Lat	Amp	Left	Lat	Amp
P 13			P 13		
N 23			N 23		

PATIENT CONSENT FORM

Study Details: A study of clinical and electrophysiological profile of vestibular function in Parkinson disease

Study Centre: Madras Medical College &
Rajiv Gandhi Government General Hospital, Chennai- 03

Patient may check (✓) these boxes:

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask questions and all my questions and doubts have been answered to my complete satisfaction. ☐

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ☐

I understand that the sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any future research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms. ☐

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, microbiological, radiological tests and lumbar puncture procedures, if deemed necessary. ☐

I hereby consent to participate in the study.

Signature/Thumb impression: Place:
Patient name and address: Date:

Signature/Thumb impression: Place:
Study investigator's name: Date:

PATIENT INFORMATION SHEET

- We are conducting a study of Clinical and electrophysiological profile of vestibular function in Parkinson disease in patients attending the Neurology services of Rajiv Gandhi Government General Hospital, Chennai.

- The purpose of the study is to assess the clinical and electrophysiological profile of the patients with Parkinson disease and healthy controls and analyze the correlation between them.

- The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

- Taking part in the study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

- The results of the study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment

Signature of the investigator **Signature of the participant**

Date:

S.No	MDC.no	Age	Sex	Duration of PD	Hoehn & Yahr stage	1.Mentation	2. Thought disorder	3. Depression	4. Motivation /initiative	5. Speech	6. Salivation	7. Swallowing	Handwriting	9 . Cutting food	10. Dressing	11. Hygiene	12. Turning in bed	13. Falling	14. Freezing	15. Walking	16. Tremor	17. Sensory symptoms	18 speech	19 . Facial expression	20. Tremor at rest
1	65/13	48	1	1	2	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	1	1
2	18/11	73	2	2	2	1	0	1	1	0	1	0	1	0	0	0	0	0	0	1	2	2	1	1	2
3	64/12	75	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	2	0	1	1
4	21/11	67	1	3	2	0	0	0	0	1	0	0	2	0	0	0	0	0	0	1	2	0	1	1	3
5	81/12	51	1	2	2	0	0	0	0	0	0	0	2	0	0	0	0	0	0	1	2	1	0	1	1
6	75/14	58	1	3	5	1	1	1	1	3	2	1	2	0	1	1	1	1	2	2	2	2	3	3	3
7	148/06	66	1	8	4	1	1	2	1	2	2	1	2	1	1	1	1	0	1	1	2	2	1	2	2
8	67/13	68	1	1	2	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	2	2	1	1	3
9	130/08	62	1	6	2	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	1	0	1	1	2
10	10/07	40	1	12	3	0	0	1	0	1	0	0	1	0	0	0	0	0	2	2	2	0	2	2	2
11	66/13	64	2	5	2	0	0	0	0	2	1	0	1	0	1	1	0	0	0	1	3	2	2	2	3
12	12/12	78	1	2	2	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	2	2	0	1	1
13	119/06	54	1	5	3	1	0	0	1	1	2	2	2	1	0	1	0	1	1	2	2	1	2	1	3
14	14/08	62	1	5	3	1	0	1	1	2	2	1	1	0	1	1	0	0	2	2	2	1	1	2	3
15	103/06	50	2	15	4	0	0	1	0	2	2	2	2	1	1	0	1	1	1	2	2	1	2	2	3
16	36/11	40	1	3	2	1	0	0	0	1	1	0	2	0	0	0	0	0	0	1	2	1	1	1	3
17	17/13	70	2	12	6	1	2	2	1	2	2	1	2	1	1	1	1	2	2	2	3	2	2	3	3
18	08/11	65	2	14	5	1	0	1	1	2	2	2	2	1	1	0	1	1	1	2	2	1	2	3	3
19	60/05	64	1	15	7	2	2	3	3	3	3	3	3	2	2	2	2	3	3	3	3	2	2	3	3
20	70/11	57	2	3	2	0	0	0	1	0	0	0	2	0	0	0	0	0	0	1	2	0	0	2	2
21	28/11	72	1	3	3	0	0	0	0	1	1	0	2	0	0	0	0	0	0	1	3	0	1	3	3
22	31/05	55	2	9	4	1	2	2	2	2	2	2	2	1	1	1	1	1	1	2	3	2	2	3	3
23	44/13	63	1	2	3	0	0	0	0	2	1	1	1	0	0	0	0	1	1	2	2	1	2	3	2
24	62/09	40	1	4	3	1	1	0	1	1	2	1	2	0	0	0	0	0	2	1	3	2	2	2	3
25	74/14	62	2	5	4	0	0	0	0	2	1	1	1	0	0	0	0	0	0	2	2	0	2	3	2
26	7/06	40	1	10	4	1	1	1	1	2	2	1	1	0	1	1	1	0	2	2	3	2	2	2	3
27	14/13	62	1	2	2	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	2	2	1	2	3
28	53/13	43	2	2	2	0	0	1	1	1	1	1	2	0	0	0	0	0	0	1	2	2	1	1	2
29	41/10	58	1	4	3	0	0	1	0	2	2	2	2	1	1	0	1	1	1	2	3	1	2	3	3
30	69/09	59	1	5	3	1	0	1	1	1	2	1	2	0	0	0	0	0	2	2	2	2	2	2	3

21. Action tremor	22. Rigidity	23. Finger taps	24. Hand grips	Movements of Hands	26.Leg Agility	27. Arise from chair	28. Posture	29. Gait	30. Postural stability	31. Body bradykinesia	32. Dyskinesia (duration)	33. Dyskinesia (disability)	34. Dyskinesia (pain)	morning dystonia	36. "offs" (predictable)	37. "offs" (unpredictable)	38. "offs" (sudden)	39. "offs" (duration)	nausea, vomiting	41. Sleep disturbance	Symptomatic orthostasis	Total score	Sitting Balance	Rises from chair	Attempts to rise
0	1	1	1	1	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	10	1	2	2
0	2	2	2	2	2	0	1	0	0	1	0	0	0	0	1	0	0	0	0	0	0	27	1	2	2
0	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	11	1	2	2
1	1	1	1	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	18	1	2	2
0	1	1	1	1	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	15	1	2	2
1	3	3	3	3	3	2	3	2	1	3	1	0	0	0	1	0	1	0	1	1	1	66	1	1	1
1	2	2	2	2	2	1	3	2	0	2	1	0	1	0	1	0	1	0	0	1	0	51	1	2	2
1	1	2	1	1	1	0	0	1	0	1	0	0	0	0	1	0	0	0	0	0	0	20	1	2	2
1	1	2	2	2	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	18	1	2	2
0	1	2	2	2	3	1	1	2	0	2	0	0	0	1	1	0	0	0	0	0	0	33	1	2	2
1	1	2	2	2	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	30	1	2	2
0	1	1	1	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	14	1	2	2
0	3	2	1	3	2	2	2	3	0	2	0	0	0	0	0	1	0	0	0	0	0	45	1	2	1
0	3	2	2	2	2	2	2	3	0	3	0	0	0	0	0	1	0	0	0	1	0	47	1	1	1
0	3	2	2	3	3	2	3	2	0	3	1	1	1	0	0	1	0	0	0	0	0	53	1	1	2
1	1	1	1	2	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	22	1	2	2
1	3	3	3	3	3	3	3	3	2	3	0	0	0	0	0	1	0	0	0	1	1	69	1	1	1
0	3	3	2	3	3	2	3	3	1	3	1	1	1	0	0	1	0	0	0	1	0	60	1	1	1
1	4	4	3	3	3	3	3	3	3	3	1	1	1	0	0	1	1	0	0	1	1	92	1	1	1
0	2	1	1	1	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	18	1	2	2
1	1	3	2	2	2	1	2	2	0	2	1	0	0	1	1	0	0	0	0	0	0	36	1	2	2
0	3	3	3	3	3	2	3	3	0	3	1	1	1	0	1	0	0	0	0	0	0	66	1	1	1
0	2	3	2	3	3	2	3	3	0	3	0	0	0	0	0	1	0	0	0	1	0	45	1	2	2
1	2	2	2	2	2	1	1	2	0	2	0	0	0	0	0	1	0	0	0	0	0	42	1	2	2
0	2	3	2	3	3	2	3	3	0	3	0	0	0	0	0	1	0	0	0	1	0	42	1	2	1
1	3	3	2	3	3	2	2	3	0	3	0	0	0	0	0	1	0	0	0	1	0	56	1	1	1
0	1	2	1	2	2	0	0	1	0	1	0	0	0	0	1	0	0	0	0	0	0	23	1	2	2
0	1	2	2	2	2	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	27	1	2	2
0	3	2	2	3	3	2	2	2	0	3	1	0	0	0	1	0	0	0	0	0	0	52	1	1	1
1	2	2	2	2	3	1	1	2	0	2	0	0	0	0	0	1	0	0	0	0	0	43	1	1	2

Immediate standing Balance	Standing balance	Nudged	Eyes closed	Turning 360 degrees	Sitting down	Balance score	Indication of gait	Step length and height	Foot clearance	Step symmetry	Step continuity	Path	Trunk	Walking stance	Gait score	Total score	Syndopa	Anticholinergics	Dopamine-agonists	COMT-inhibitor	Neuroleptics	Antidepressant
2	2	2	1	2	2	16	1	2	2	1	1	2	2	1	12	28	1	1	0	0	0	0
2	2	2	1	1	2	15	1	1	1	0	1	2	2	0	8	23	1	1	0	0	0	q
2	2	2	1	2	2	16	1	2	2	1	1	2	2	1	12	28	1	1	0	0	0	0
2	2	2	1	1	2	15	1	2	2	1	1	2	2	1	12	27	1	1	0	0	0	0
2	2	2	1	2	2	16	1	2	2	1	1	2	2	1	12	28	1	1	0	0	0	0
1	1	1	1	0	1	8	0	0	0	1	1	2	2	0	6	14	1	1	0	0	0	1
2	2	2	1	2	2	16	1	2	2	1	1	2	2	1	12	28	1	1	0	0	0	0
2	2	2	1	1	2	15	1	1	2	0	1	2	2	0	9	24	1	1	0	0	0	0
2	2	2	1	1	2	15	1	2	2	0	1	2	2	0	10	25	1	1	0	0	0	0
2	2	2	1	1	2	15	1	1	1	0	0	2	1	0	6	21	1	1	0	0	0	0
2	2	2	1	2	2	16	1	2	2	1	1	2	2	1	12	28	1	1	0	0	0	0
2	2	2	1	1	2	15	1	2	2	0	1	2	2	1	11	26	1	1	0	0	0	1
2	2	2	1	0	2	13	1	1	1	1	1	2	2	1	10	23	1	1	0	0	0	0
2	2	2	1	0	2	12	1	1	1	0	1	2	2	0	8	22	1	1	0	0	0	1
2	2	2	1	0	2	13	1	1	1	0	0	2	2	0	7	20	1	1	0	0	0	1
2	2	2	1	2	2	16	1	1	2	1	1	2	2	1	11	27	1	1	0	0	0	0
1	1	0	1	0	1	7	0	0	0	1	0	2	1	0	4	11	1	1	0	0	0	1
1	2	1	1	0	2	10	1	1	0	0	1	2	1	0	6	16	1	1	0	0	0	1
0	1	0	0	0	1	5	0	0	0	1	1	2	1	0	5	10	1	1	0	0	0	1
2	2	2	1	2	2	16	1	2	2	1	1	2	2	1	12	28	1	1	0	0	0	0
2	2	1	1	1	2	14	1	2	2	0	1	2	2	1	11	23	1	1	0	0	0	0
1	2	2	1	0	2	11	1	0	1	0	0	2	2	0	6	17	1	1	0	0	1	1
2	2	2	1	1	2	15	1	1	1	0	1	2	2	1	9	24	1	1	0	0	0	0
2	2	1	1	0	2	13	1	1	1	1	1	2	2	1	10	23	1	1	0	0	0	0
2	2	2	1	0	2	13	1	1	1	0	1	2	2	1	9	22	1	1	0	0	0	0
1	2	2	1	0	2	11	1	1	0	0	0	2	2	0	6	17	1	1	0	0	0	1
2	2	2	1	1	2	15	1	1	2	0	1	2	2	0	9	24	1	1	0	0	0	1
2	2	2	1	1	2	15	1	2	2	0	1	2	2	0	10	25	1	1	0	0	0	1
2	2	1	1	1	2	12	1	1	0	0	1	2	2	1	8	20	1	1	0	0	0	1
2	2	1	1	0	2	12	1	1	1	0	1	2	2	1	9	21	1	1	0	0	0	1

VEMP of Cases						VEMP of Controls						
LT-VEMP	RT- VEMP	LT- p13	LT-n23	RT- p13	RT- n23	S.no	SEX	AGE	LT- p13	LT-n23	RT- p13	RT- n23
1	1	11.0	16.7	10.8	16.6	1	1	28	10.5	13.2	10.6	13.4
1	1	12.8	21.8	12.7	21.9	2	1	65	12.0	20.1	12.8	19.2
1	1	12.6	21.6	12.6	22	3	1	54	13.1	18.5	12.5	19.4
1	1	12.6	21.9	12.7	21.7	4	1	43	10.5	19.1	11.5	20.1
1	1	12.6	21.8	12.5	21.7	5	2	62	14.6	21.9	14.4	22.4
0	0	0	0	0	0	6	1	45	11.9	17.2	11.7	15.9
1	0	13.2	17.1	0	0	7	1	71	13.2	21.8	13.3	21.7
1	1	12.7	21.9	12.7	21.6	8	1	61	14.1	21.8	14.0	21.8
1	1	13	21.8	12.6	21.8	9	1	54	12.7	21.3	12.7	21.6
1	1	13.1	21.8	11.8	21.3	10	2	66	11.0	20.6	12.1	19.9
1	1	12.7	21.9	12.7	21.6	11	1	58	12.8	21.8	12.7	21.9
1	1	14.1	21.8	14.0	21.8	12	2	63	12.6	21.6	12.6	22
1	1	13.1	19.4	13.1	19.3	13	1	43	9.2	20.5	9.5	19.1
1	1	11.9	19.8	12.5	19.8	14	1	56	11.9	15.1	12.0	15.7
1	1	9.2	20.5	9.5	19.1	15	1	70	10.9	19.1	11.5	20.1
1	1	11.9	15.1	12.0	15.7	16	1	54	13.7	19.5	14.2	20.3
0	0	0	0	0	0	17	2	65	13.1	18.5	12.5	19.4
0	0	0	0	0	0	18	1	52	10.5	19.1	11.5	20.1
1	1	12.1	16.1	12.3	16.3	19	2	48	13	21.8	12.6	21.8
1	1	12.7	21.8	12.7	21.8	20	2	38	13.1	21.8	11.8	21.3
1	1	11.0	20.6	12.5	19.9	21	1	46	12.7	21.9	12.7	21.6
1	1	11.2	19.2	12.5	19.2	22	2	69	13.2	17.1	12.1	19.9
0	0	0	0	0	0	23	1	68	13.2	21.8	13.3	21.7
0	0	0	0	0	0	24	1	58	10.5	19.1	11.5	20.1
1	1	13.7	19.5	14.2	20.3	25	2	66	11.0	16.7	10.8	16.6
0	0	0	0	0	0	26	1	59	12.8	21.8	12.7	21.9
1	1	11.5	19.7	11.6	17.0	27	1	64	12.6	21.6	12.6	22
0	0	0	0	0	0	28	1	47	12.3	21.9	12.7	21.7
0	0	0	0	0	0	29	2	52	14.6	21.2	14.4	22.4
1	1	10.2	20.1	10.2	20.1	30	2	58	11.9	17.2	11.7	15.9

Clinical and electrophysiological profile of vestibular function in parkinson disease

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INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
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Fax: 044 25363970

CERTIFICATE OF APPROVAL

To

Dr.R.Ravichandran,
Postgraduate in Neurology,
Institute of Neurology,
Madras Medical College, Chennai-3.

Dear **Dr.R.Ravichandran,**

The Institutional Ethics Committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "**Clinical and Electrophysiological Profile of Vestibular Function in Parkinson Disease** " No.20022014.

The following members of Ethics Committee were present in the meeting held on 04.02.2014 conducted at Madras Medical College, Chennai-3.

1.	Dr. G. Sivakumar, MS FICS FAIS	-- Chairperson
2.	Prof. B.Kalaiselvi, MD Vice Principal, MMC, Ch-3	-- Member Secretary
3.	Prof. Ramadevi, Director i/c, Instt. of Biochemistry, Chennai.	-- Member
4.	Thiru. S. Govindasamy, BA., BL	-- Lawyer
5.	Tmt.Arnold Saulina, MA MSW	-- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

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INSTITUTIONAL ETHICS COMMITTEE
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EC Reg No.ECR/270/Inst./TN/2013
Telephone No : 044 25305301
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CERTIFICATE OF APPROVAL

To

Dr.R.Ravichandran,
Postgraduate in Neurology,
Institute of Neurology,
Madras Medical College, Chennai-3.

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